

UNITED STATES DISTRICT COURT
DISTRICT OF NEVADA

4 AMARIN PHARMA, INC., and :
5 AMARIN PHARMACEUTICALS :
6 IRELAND LIMITED, :
7 Plaintiffs, :
8 : No. 2:16-cv-02525-MMD-NJK
9 : January 28, 2020
10 : Reno, Nevada
11 : Volume 7
12 :
13 Defendants. :

TRANSCRIPT OF BENCH TRIAL

APPEARANCES:

FOR THE PLAINTIFFS: MEAGAN P. KEANE, CHRISTOPHER N. SIPES, MICHAEL KENNEDY, JEFFREY ELIKAN, JOSEPH KENNEDY, ELAINA M. WHITT, BARBARA KURYS, HAN PARK, DANIEL J. FARNOLY and ERIC R. SONNENSCHEIN
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Reported by: Kathryn M. French, CCR #392, RPR
Official Reporter
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Reno, Nevada

(Appearances continue on next page.)

1 APPEARANCES CONTINUED:

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08:37:38 10 FOR DEFENDANT DR. CONSTANCE S. HUTTNER and
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08:02:41 1 RENO, NEVADA, TUESDAY, JANUARY 28, 2020, 8:30 A.M.
08:03:04 2 --oo--
08:30:17 3 THE COURT: Good morning. Please be seated.
08:30:20 4 MR. ELIKAN: Your Honor, good morning.
08:32:11 5 THE COURT: Good morning. Are you ready?
08:32:13 6 MR. ELIKAN: May I proceed?
08:32:15 7 THE COURT: Yes. Thank you.

8 PETER PAUL TOTH, M.D.,
9 recalled as a witness on behalf of the plaintiffs,
previously sworn, testified further as follows:

10 DIRECT EXAMINATION RESUMED

11 BY MR. ELIKAN:

08:32:17 12 Q Yesterday we were discussing the JELIS trial when we
08:32:20 13 broke. I want to turn now to PX 272, the publication by
08:32:28 14 Dr. Bhatt the REDUCE-IT study we looked at before.

08:32:33 15 MR. ELIKAN: Can we have Figure 4 on page 10.

08:32:33 16 BY MR. ELIKAN:

08:32:36 17 Q How do these results compare to the JELIS results?
08:32:40 18 A Well, what we see here, counsel, are across-the-board
08:32:45 19 significant reductions in all of the cardiovascular endpoints
08:32:49 20 evaluated, whereas within JELIS, the primary composite
08:32:54 21 endpoint.

08:32:55 22 And the endpoint unstable angina, only those two are
08:33:00 23 reduced.

08:33:01 24 Q And you explained yesterday that unstable angina is the
08:33:06 25 driver of the other endpoint, right?

08:33:08 1 A Yes.

08:33:09 2 Q And these differences, all of the cardiovascular

08:33:13 3 differences, those are all statistically significant?

08:33:17 4 A Yes.

08:33:20 5 MR. ELIKAN: Can we pull up the second full

08:33:22 6 paragraph in the right-hand column on page 9 and highlight the

08:33:27 7 first sentence.

08:33:27 8 BY MR. ELIKAN:

08:33:33 9 Q What does Dr. Bhatt state here about how Vascepa results

08:33:38 10 stand apart from other results achieved with other drugs?

08:33:44 11 A "The results of REDUCE-IT stand apart from

08:33:47 12 the negative findings of several contemporary trials

08:33:49 13 of other agents that also lower triglyceride levels,

08:33:53 14 including other omega-3 fatty acids, extended release

08:33:58 15 niacin, fenofibrate, and cholesterol ester transfer

08:33:58 16 protein inhibitors."

08:34:09 17 Q Do you recall that Dr. Heinecke testified that there was

08:34:11 18 not a failure of others to reduce cardiovascular risk with a

08:34:15 19 triglyceride-lowering agent?

08:34:16 20 A Yes.

08:34:17 21 Q Is Dr. Heinecke's position consistent with Dr. Bhatt's

08:34:24 22 observations?

08:34:25 23 A No.

08:34:26 24 Q Proceeding to the next sentence, does Dr. Bhatt offer a

08:34:36 25 clear explanation for why clinical trials fail to demonstrate

08:34:39 1 a cardiovascular benefit or was it for him still a matter of
08:34:42 2 uncertainty? What did he have to say?

08:34:44 3 A He reflects some uncertainty. He states,

08:34:49 4 Q "It is not known whether the lack of benefit
08:34:50 5 from omega-3 fatty acids in previous trials may be
08:34:55 6 attributable to the low dose or the low ratio of EPA
08:35:00 7 to DHA."

08:35:01 8 Q Still looking at the same paragraph I'm going to ask you
08:35:04 9 about an additional sentence further down the paragraph
08:35:09 10 beginning with "although the dose."

08:35:12 11 What does Bhatt have to say here about how the dose
08:35:18 12 in JELIS compared to the dose in REDUCE-IT?

08:35:22 13 A Dr. Bhatt notes,

08:35:24 14 Q "Although the dose of EPA administered in
08:35:27 15 JELIS (1.8 grams daily) was lower than the
08:35:32 16 EPA-equivalent dose used in REDUCE-IT (4 grams
08:35:35 17 daily), it resulted in a plasma EPA level
08:35:39 18 (170 micrograms per milliliter in a Japanese
08:35:44 19 population) similar to that attained in a previous
08:35:47 20 12-week lipid study in which a total daily dose of 4
08:35:51 21 grams of icosapent ethyl was used in a Western
08:35:54 22 population (183 micrograms per milliliter) and
08:35:59 23 similar to that attained in the current trial."

08:36:01 24 Q So my question was how does the dose in JELIS compare to
08:36:06 25 the dose administered in REDUCE-IT.

08:36:09 1 A In terms of attained EPA levels in serum --

08:36:13 2 Q Before we get to the serum, what was the dose

08:36:16 3 administered in the two trials?

08:36:17 4 A Okay. In REDUCE-IT, it was 4 grams, in JELIS, it was

08:36:22 5 1.8 grams.

08:36:23 6 Q Now, let's turn to the serum. Maybe you can unpack the

08:36:27 7 passage you read. What is this saying about the serum levels?

08:36:30 8 A That they were very close, 170 micrograms per milliliter

08:36:35 9 of EPA in JELIS, and 183 micrograms per milliliter in the

08:36:49 10 MARINE trial, and similar to what was seen in REDUCE-IT.

08:36:52 11 Q Do you see a reference to -- citation to references 25

08:36:56 12 and 26?

08:36:58 13 A I do.

08:36:59 14 MR. ELIKAN: Let's take a look at those for a

08:37:01 15 second as they're listed at the end the article.

08:37:04 16 Can we pull up those references on page 12.

08:37:04 17 BY MR. ELIKAN:

08:37:14 18 Q Based on the dates of publication, would these references

08:37:18 19 have been available to the person of ordinary skill in the art

08:37:20 20 in March 2008?

08:37:23 21 A They were published in 2011 and 2016, so the answer is

08:37:28 22 no.

08:37:29 23 Q Do you recall that yesterday we looked at the Yokoyama

08:37:33 24 article?

08:37:33 25 A Yes.

08:37:34 1 Q Where it acknowledged that an exclusively Japanese
08:37:39 2 population was studied?

08:37:41 3 A Yes.

08:37:42 4 MR. ELIKAN: I want to turn back to that. Can
08:37:44 5 we go to DX 1553 and page 8, and I want to pull up on the
08:37:51 6 screen the last paragraph of the paper and highlight the
08:37:54 7 second to last sentence.

08:37:54 8 BY MR. ELIKAN:

08:37:58 9 Q What did the author state here about the consequence of
08:38:02 10 the study population being exclusively Japanese?

08:38:05 11 A Dr. Yokoyama notes that,

08:38:07 12 Q "Because our population was exclusively
08:38:10 13 Japanese, we cannot generalize our results to other
08:38:13 14 populations."

08:38:14 15 MR. ELIKAN: And I want to go now to page 7 and
08:38:17 16 highlight the statement at the bottom of the left-hand column
08:38:21 17 which carries over to the top of the right-hand column.

08:38:21 18 BY MR. ELIKAN:

08:38:32 19 Q What did the author state here about how the average
08:38:36 20 Japanese diet compares to the diet of people in other
08:38:39 21 countries?

08:38:40 22 A "In Japan, death from coronary artery disease
08:38:45 23 is rare, and the average dietary intake of fish is
08:38:48 24 about five times higher than that in other
08:38:51 25 countries."

08:38:53 1 Q Does fish contain DHA?

08:38:55 2 A Yes.

08:38:56 3 Q If a person of ordinary skill in the art wanted to

08:39:02 4 formulate an omega-3 for other populations that don't eat as

08:39:07 5 much fish, and believed it was necessary to mimic the

08:39:12 6 composition of omega-3 fatty acids that Japanese people

08:39:16 7 consume throughout the day, would that person have included

08:39:20 8 substantial amounts of DHA?

08:39:22 9 A Yes.

08:39:22 10 Q And why is that?

08:39:25 11 A Because they would try to mimic -- is a good word -- the

08:39:33 12 dietary reconditions of the people in Japan who participated

08:39:38 13 in this study.

08:39:39 14 The supplement was EPA alone, but because they eat

08:39:42 15 five times as much fish as people in other countries, they're

08:39:47 16 still taking in a very substantial amount of DHA daily.

08:39:49 17 Q Have you prepared a slide showing the doses used for

08:39:53 18 omega-3 fatty acid cardiovascular outcome trials underway as

08:40:02 19 of March 2008?

08:40:05 20 A Yes.

08:40:05 21 MR. ELIKAN: Can we have PDX 6-31.

08:40:05 22 BY MR. ELIKAN:

08:40:08 23 Q Before we walk through the specifics, are these the same

08:40:12 24 trials you discussed earlier, that is, yesterday, the omega-3

08:40:15 25 fatty acid cardiovascular outcome trials underway as of March

08:40:18 1 **2008?**

08:40:20 2 A **Yes, counsel.**

08:40:20 3 Q **And are the source materials the same?**

08:40:22 4 A **Yes.**

08:40:23 5 Q **And what were the doses that were being studied as of**

08:40:27 6 **March 2008?**

08:40:29 7 A **Well, you see five trials used one gram daily, one trial**

08:40:34 8 **used 400 milligrams daily, one used 600 milligrams daily, and**

08:40:39 9 **another used 2.4 grams daily.**

08:40:42 10 Q **Did any of the outcome trials underway as of March 2008**

08:40:48 11 **on omega-3 fatty acids use 4 grams?**

08:40:53 12 A **No.**

08:40:54 13 MR. ELIKAN: **We move for the admission of PDX**

08:40:57 14 **6-31 under Federal Rule of Evidence 1006.**

08:40:59 15 MR. KLEIN: **No objection.**

08:41:01 16 THE COURT: **PDX 6-31 is admitted.**

08:41:01 17 (Plaintiffs' Exhibit 6-31 received in

08:41:01 18 **evidence.)**

BY MR. ELIKAN:

08:41:06 19 Q **What, if anything, do the doses used in these**

08:41:09 20 **cardiovascular outcome trials suggest about whether it would**

08:41:13 21 **have been obvious to use 4 grams of EPA to lower**

08:41:17 22 **cardiovascular risk?**

08:41:18 23 A **Well, it suggests that no one believed that 4 grams was**

08:41:21 24 **the magic bullet here. People were using different doses**

08:41:25 25 **because, as I said, they were feeling their way through the**

08:41:28 1 **dark.**

08:41:28 2 MR. ELIKAN: Let's go back to PDX 6-32, and
08:41:33 3 **skepticism.**

08:41:33 4 **BY MR. ELIKAN:**

08:41:35 5 Q In your work on this case, did you review materials that
08:41:38 6 reflected skepticism about whether or not omega-3 fatty acids
08:41:43 7 would provide a cardiovascular benefit?

08:41:45 8 A Yes.

08:41:46 9 Q Do you recall yesterday we looked at a statement in the
08:41:50 10 Cochrane collaboration, PX 953, that Omega-3s, and I'm
08:41:56 11 quoting, "probably are not useful for preventing or treating
08:41:59 12 cardiovascular disease"?

08:42:01 13 A Yes.

08:42:02 14 Q And do you recall looking at a statement in an article by
08:42:07 15 Dr. Aung, PX 954, that there is, quote,
08:42:11 16 "No support for current recommendations for
08:42:14 17 the use of such supplements in people with a history
08:42:17 18 of coronary heart disease"?

08:42:20 19 A Yes.

08:42:23 20 Q Do you consider these examples of skepticism?

08:42:27 21 A Yes.

08:42:27 22 Q Were you, Dr. Toth, as skeptical as some other people
08:42:32 23 were?

08:42:32 24 A No, I was more optimistic. I was more hopeful. And I
08:42:38 25 was still hoping that the omega-3s would be able to

08:42:43 1 demonstrate benefit.

08:42:44 2 Q And in being hopeful, do you believe you were in the
08:42:47 3 majority or the minority?

08:42:49 4 A Oh, I was in the minority.

08:42:51 5 Q Are there other materials you have reviewed in this case
08:42:54 6 that reflect skepticism about the potential of omega-3 fatty
08:43:00 7 acids to lower cardiovascular risk before REDUCE-IT?

08:43:04 8 A Yes.

08:43:04 9 Q Let's turn to PX 951. And what is this?

08:43:08 10 A This is an article by Adam Feuerstein entitled "Amarin
08:43:16 11 Fish Oil Capsule Shows Dramatic Benefit For Cardiovascular
08:43:20 12 Patients, Potentially Upending Market."

08:43:23 13 Q What's the date of the article?

08:43:25 14 A September 24th, 2018.

08:43:27 15 MR. ELIKAN: Your Honor, we move for admission
08:43:29 16 of PX 951.

08:43:29 17 MR. KLEIN: No objection.

08:43:29 18 BY MR. ELIKAN:

08:43:29 19 Q Let's turn to --

08:43:29 20 THE COURT: 951?

08:43:36 21 MR. ELIKAN: Yes, I'm sorry, Your Honor.

08:43:36 22 THE COURT: Exhibit 951 is admitted.

08:43:36 23 (Plaintiffs' Exhibit 951 received in
08:43:36 24 evidence.)

BY MR. ELIKAN:

08:43:42 25 Q Turning to the sixth paragraph on page 2, what did

08:43:46 1 Dr. Ethan Weiss, the cardiologist at UCSF, have to say about
08:43:52 2 the Vascepa study?

08:43:54 3 A "I thought the Vascepa study would be
08:43:56 4 negative, colored by all the prior failed studies, so
08:43:59 5 I'm surprised. I'm willing to eat my shoe on this
08:44:02 6 one. This could be really beneficial to people."

08:44:07 7 Q And in the last paragraph on page 3, what did Dr. Norman
08:44:16 8 Lepor of Cedars-Sinai Medical Center have to say?

08:44:21 9 A "I went into this study not convinced that
08:44:24 10 Vascepa would make a difference, but these results
08:44:26 11 will definitely change my practice and the way I
08:44:29 12 treat patients."

08:44:30 13 Q Do you consider these examples of skepticism?

08:44:33 14 A Yes.

08:44:33 15 Q In general, have the REDUCE-IT trial results now been
08:44:37 16 embraced by the medical community?

08:44:39 17 A Yes.

08:44:40 18 Q Do you recall that Dr. Heinecke testified that there was
08:44:47 19 no relevant skepticism that EPA would reduce cardiovascular
08:44:52 20 risk?

08:44:53 21 A Yes.

08:44:53 22 Q And in light of all the materials that you've reviewed,
08:44:56 23 do you agree with Dr. Heinecke that there was no relevant
08:45:00 24 skepticism that EPA would reduce cardiovascular risk?

08:45:04 25 A No.

08:45:05 1 MR. ELIKAN: Let's turn back to PDX 6-33. I
08:45:11 2 want to turn now to Unexpected Results.

08:45:11 3 BY MR. ELIKAN:

08:45:17 4 Q You testified earlier that the REDUCE-IT results apply
08:45:20 5 equally to a population with severe hypertriglyceridemia
08:45:26 6 because, among other things, we knew from MARINE there would
08:45:29 7 be no substantial rise in LDL-C.

08:45:32 8 Do you recall that testimony?

08:45:33 9 A Yes.

08:45:33 10 Q Was there any parallel study that existed in March 2008
08:45:39 11 that would have told the person of ordinary skill in the art
08:45:44 12 that when Epadel is given to a patient population with severe
08:45:48 13 hypertriglyceridemia, there will be no substantial rise in
08:45:51 14 LDL-C?

08:45:54 15 A No.

08:45:55 16 Q Do you recall that Dr. Heinecke testified that JELIS
08:45:58 17 reported a 19 percent reduction in cardiovascular risk?

08:46:01 18 A Yes.

08:46:02 19 Q And accepting that risk reduction at face value, would
08:46:07 20 the person of ordinary skill in the art have expected -- would
08:46:13 21 they have had reason to expect that this risk reduction
08:46:16 22 reported in patients with, I believe you said a mean baseline
08:46:19 23 triglyceride level of 153?

08:46:21 24 A Yes.

08:46:22 25 Q -- that it would apply to patients with severe

08:46:25 1 **hypertriglyceridemia?**

08:46:26 2 A **No.**

08:46:28 3 Q **Triglycerides over 500.**

08:46:30 4 A **No.**

08:46:30 5 Q **And why not?**

08:46:31 6 A **Because a person of ordinary skill in the art as of March 2008 would have understood that the response in LDL for patients below 500 on their triglycerides and above 500 were distinctly different.**

08:46:51 10 MR. ELIKAN: I'd like to pull up, again, PX 272, the Bhatt publication, and go to page 10 and back to Figure 4.

08:47:02 12 And, Mr. Brooks, can you highlight Fatal Or Nonfatal Stroke.

08:47:06 14 BY MR. ELIKAN:

08:47:12 15 Q **What's the risk reduction shown for stroke?**

08:47:15 16 A **Twenty-eight percent, and it is statistically significant.**

08:47:19 18 Q **Would this result have been expected after JELIS?**

08:47:24 19 A **No.**

08:47:25 20 MR. ELIKAN: Let's look at JELIS on stroke. Can we have -- DX 1553, please, and Figure 3 on page 5, and I want to look at the analysis on stroke. It starts at the bottom.

08:47:46 23 And, Mr. Brooks, can you highlight the stroke line.

08:47:49 24

08:47:49 25

08:47:49 1 BY MR. ELIKAN:

08:47:53 2 Q What was reported in terms of risk reduction for stroke
08:47:58 3 in the JELIS study?

08:48:00 4 A Well, the hazard ratio is 1.02, statistically not
08:48:05 5 significant, and you'll notice that the point is virtually
08:48:09 6 straddling unity, that vertical bar. So there was no impact
08:48:15 7 on stroke in the JELIS trial.

08:48:16 8 Q What does it mean that it's a number that's higher than
08:48:20 9 1?

08:48:20 10 A Well, if it's higher than 1, that means there's hazard
08:48:25 11 that it would increase that specific endpoint. But we can't
08:48:28 12 conclude here that stroke went up by 2 percent because it's
08:48:33 13 not statistically significant.

08:48:34 14 Q Is a statistically significant reduction in stroke of
08:48:42 15 28 percent an important clinical benefit?

08:48:44 16 A Counsel, it is enormously important because it's over and
08:48:47 17 above that observed with statin therapy.

08:48:50 18 And if we think about this, stroke is one of the
08:48:52 19 most dreaded cardiovascular complications of all because it
08:48:56 20 can leave a loved one with the inability to speak, walk,
08:49:01 21 think, it could change their personality.

08:49:04 22 Yes, it's of enormous, enormous importance.

08:49:11 23 Q Do you consider this difference, 28 percent and zero, one
08:49:23 24 of degree or one of kind?

08:49:25 25 A Well, I think it speaks for itself. It's one of kind.

08:49:29 1 Q And for patients who don't experience a stroke, who would
08:49:35 2 have without Vascepa, is that a difference in kind or in
08:49:39 3 degree?

08:49:40 4 A It's a difference in kind.

08:49:42 5 Q Let's go back to PX 272 and back to Figure 4. I'm going
08:49:51 6 to look at the cardiovascular death endpoint.

08:49:55 7 What did REDUCE-IT report with respect to the effect
08:50:00 8 of Vascepa on cardiovascular death?

08:50:04 9 A REDUCE-IT reported a 20 percent relative risk reduction
08:50:09 10 in cardiovascular death that was statistically significant at
08:50:15 11 P equal to .03.

08:50:17 12 Q Would that result have been expected based on JELIS?

08:50:22 13 A No, counsel.

08:50:26 14 MR. ELIKAN: I'd like to go back to Yokoyama,
08:50:29 15 DX 1553, and page 5, Figure 3, and can we highlight the
08:50:39 16 coronary death entry.

08:50:39 17 BY MR. ELIKAN:

08:50:41 18 Q What did JELIS report in terms of the risk of
08:50:44 19 cardiovascular death?

08:50:47 20 A There was a 6 percent trend for reduction. There's a
08:50:50 21 slight leftward shift, left of unity. But, it didn't even
08:50:55 22 come close to statistical significance with a P value of .81.

08:51:04 23 Q It looks like this line through which the dot runs is
08:51:08 24 very wide. What does that signify?

08:51:10 25 A That means there's great uncertainty about how accurate

08:51:15 1 that estimate is.

08:51:18 2 Q Is REDUCE-IT significant reduction in cardiovascular
08:51:24 3 death a difference in kind or in degree compared to JELIS'
08:51:29 4 nonsignificant risk reduction on cardiovascular death?

08:51:33 5 A It is a difference in kind. This has never been shown
08:51:37 6 before when using an adjutant therapy over and above a statin.

08:51:42 7 We've seen numerous trials with adjutant therapies
08:51:47 8 on top of a statin and none of them have been able to
08:51:50 9 demonstrate an incremental reduction in mortality over and
08:51:55 10 above a statin.

08:51:56 11 This is a profound difference in kind. Death is it,
08:52:00 12 there is no second chance. Reducing death by 20 percent for
08:52:07 13 cardiovascular events over and above a statin is a landmark
08:52:11 14 achievement.

08:52:12 15 Q In summary, do you agree with Dr. Heinecke that the
08:52:16 16 cardiovascular benefits shown in REDUCE-IT were expected?

08:52:23 17 A No, they were not expected. I think the evidence speaks
08:52:26 18 for itself.

08:52:28 19 Q And do you agree with him in summary that the results of
08:52:33 20 REDUCE-IT were merely a difference in degree as compared to
08:52:38 21 JELIS rather than one -- than a difference in kind?

08:52:41 22 A No, I do not agree with that assessment.

08:52:44 23 Q I want to go back to PDX 6-34. Are you ready to discuss
08:52:52 24 praise?

08:52:53 25 A Yes, counsel.

08:52:54 1 MR. ELIKAN: Can we pull up PDX 6-10 that we
08:52:57 2 discussed earlier.

08:52:57 3 BY MR. ELIKAN:

08:52:59 4 Q In your opinion, are the references listed in PDX 6-10
08:53:04 5 that you testified about yesterday, PX 952, PX 902, and PX
08:53:13 6 714, examples of praise for REDUCE-IT?

08:53:17 7 A Yes.

08:53:26 8 Q You testified earlier that the cardiovascular benefits in
08:53:30 9 REDUCE-IT were independent of the triglyceride levels of the
08:53:34 10 participants and that severely hypertriglyceridemic patients
08:53:42 11 enjoy the same benefits. Do you recall that?

08:53:44 12 A Yes.

08:53:45 13 Q So my question to you is do you read the praise in these
08:53:48 14 articles as equally applicable to patients with severe
08:53:53 15 hypertriglyceridemia?

08:53:54 16 A Yes.

08:53:54 17 Q Do you recall that Dr. Heinecke testified that there is
08:54:03 18 no nexus between the benefits observed in REDUCE-IT and the
08:54:08 19 asserted claims?

08:54:09 20 A Yes.

08:54:09 21 Q Do you agree with him?

08:54:10 22 A No.

08:54:11 23 Q Do you recall that Dr. Heinecke first disputed nexus on
08:54:17 24 the ground that the asserted claims are directed to a method
08:54:20 25 of reducing triglycerides, but that cardiovascular risk

08:54:25 1 reduction in REDUCE-IT was not the result of triglyceride
08:54:30 2 lowering?

08:54:30 3 A Yes.

08:54:31 4 Q So I want to now turn to the Bhatt article again, PX 272
08:54:38 5 at page 10, starting at the bottom of the left-hand column and
08:54:44 6 carrying over to the right-hand column.

08:54:47 7 Does this passage beginning with "these
08:54:55 8 observations," does it rule out the possibility that some of
08:54:57 9 the cardiovascular reduction may be the result of triglyceride
08:55:04 10 lowering?

08:55:04 11 A No.

08:55:05 12 "These observations suggest that at least
08:55:07 13 some of the effect of icosapent ethyl that resulted
08:55:09 14 in a lower risk of ischemic events than that with
08:55:15 15 placebo may be explained by metabolic effects other
08:55:18 16 than the reduction of triglycerides,"
08:55:19 17 but he doesn't rule it out.

08:55:26 18 Q And setting aside whether triglyceride lowering explains
08:55:31 19 any of the cardiovascular benefits observed in REDUCE-IT, will
08:55:36 20 administering the claimed treatment method of 4 grams of high
08:55:42 21 purity EPA result in patients receiving the cardiovascular
08:55:46 22 benefits observed in REDUCE-IT?

08:55:48 23 A Yes.

08:55:49 24 Q Do you recall that Dr. Heinecke also testified that
08:55:54 25 there's no nexus between the REDUCE-IT findings and the

08:55:57 1 asserted claims because REDUCE-IT did not begin to show a
08:56:01 2 divergent of reduction in cardiovascular events until year one
08:56:07 3 rather than at 12 weeks?

08:56:08 4 A Yes.

08:56:08 5 Q In your opinion, does the fact that there was no
08:56:12 6 statistically significant reduction in cardiovascular events
08:56:16 7 in REDUCE-IT at 12 weeks mean that there is no cardiovascular
08:56:22 8 advantage to a patient who has taken Vascepa for 12 weeks
08:56:27 9 compared to a patient who hasn't?

08:56:29 10 A Well, as a clinician, I have to say you have to start
08:56:33 11 somewhere. You have to initiate treatment if you want to
08:56:36 12 expect benefit downstream.

08:56:38 13 We know from MARINE that within three months you
08:56:40 14 will most certainly induce biochemical metabolic changes in
08:56:46 15 that patient's lipoprotein physiology that are beneficial,
08:56:51 16 reducing triglycerides, keeping LDL neutral, reducing apo B.

08:56:57 17 And MARINE also demonstrated that multiple different
08:57:01 18 inflammatory mediators also decrease. These would all be seen
08:57:04 19 as beneficial and all have been tied to cardiovascular
08:57:07 20 benefit.

08:57:08 21 Q You said that these benefits were observed at three
08:57:12 22 months. Were they observed at 12 weeks in MARINE?

08:57:15 23 A Yes, I'm sorry, 12 weeks.

08:57:17 24 Q Does that mean that the patient is getting closer to a
08:57:23 25 point where there will be -- where that patient will be at the

08:57:28 1 point in a study in which there are observable differences?

08:57:34 2 A Yes, we know that with any drug it takes time to accrue

08:57:38 3 enough benefit, enough physiologic change or anatomical change

08:57:44 4 so that you can reserve reductions in cardiovascular events.

08:57:46 5 Q Do you also need a study to have enough events occur in

08:57:52 6 order to see a divergence --

08:57:55 7 A Yes.

08:57:56 8 Q -- between two arms?

08:57:57 9 A You do.

08:57:57 10 Q Now, do you recall that Dr. Heinecke testified that the

08:58:01 11 patients in REDUCE-IT were on statin therapy while some of the

08:58:07 12 asserted claims specify that the medication is administered

08:58:11 13 without concomitant lipid-altering therapy?

08:58:16 14 Do you recall that testimony?

08:58:17 15 A Yes.

08:58:17 16 Q I want to ask you some questions about that.

08:58:19 17 What's the primary mechanism by which statins lower

08:58:24 18 cardiovascular risk?

08:58:25 19 A LDL cholesterol reduction.

08:58:28 20 Q Does Vascepa lower cardiovascular risk by lowering LDL-C?

08:58:34 21 A No.

08:58:34 22 Q Is it the case, then, that Vascepa and statins lower

08:58:41 23 cardiovascular risk through different mechanisms?

08:58:45 24 A Yes, that is the best explanation.

08:58:47 25 Q And what, if anything, does that suggest about whether

08:58:50 1 patients taking Vascepa will derive a benefit, even if they're
08:58:55 2 not on statins?

08:58:56 3 A It would strongly suggest that they would derive benefit
08:59:00 4 even if they're not on statins.

08:59:04 5 Q Given that fact, do you agree with Dr. Heinecke that
08:59:08 6 there's no nexus between the REDUCE-IT benefits and the claims
08:59:11 7 that require patients not to be on concurrent statin therapy?

08:59:15 8 A No.

08:59:16 9 Q I want to turn to the remaining asserted claims.

08:59:20 10 Do the reasons you've testified that claim 1 of the
08:59:25 11 '728 patent would not have been obvious apply to the other
08:59:28 12 asserted claims as well?

08:59:29 13 A Yes.

08:59:30 14 Q Some of the asserted claims other than claim 1 of the
08:59:37 15 '728 patent specify that the claimed treatment must effect a
08:59:41 16 reduction in apo B. Have you prepared a slide that identifies
08:59:45 17 the claims that discuss reductions in apo B?

08:59:49 18 A Yes.

08:59:49 19 Q Can we have PDX 6-35.

08:59:53 20 What are the claims and limitations relating to apo
08:59:57 21 B?

08:59:57 22 A Claim 8 of the '677 patent states "to.

09:00:00 23 Effect a reduction in apolipoprotein B compared to
09:00:04 24 placebo control."

09:00:05 25 Claim 5 of the '929 patent states "effective to

09:00:10 1 **reduce apolipoprotein B."**

09:00:13 2 **And claim 14 of the '715 patent states "to effect a**
09:00:17 3 **statistically significant reduction in apolipoprotein B."**

09:00:24 4 Q **You testified yesterday that Lovaza did not reduce apo B**
09:00:29 5 **in patients with very high triglycerides. In your opinion,**
09:00:32 6 **would a person of ordinary skill in the art have reasonably**
09:00:36 7 **expected that administering 4 grams of EPA in March 2008,**
09:00:42 8 **would reduce apo B in patients with very high triglycerides?**

09:00:46 9 A **No, they have no foundation for that.**

09:00:48 10 Q **Do you recall that Dr. Heinecke testified that a person**
09:00:54 11 **of ordinary skill in the art would have reasonably expected**
09:00:58 12 **that 4 grams of EPA would reduce apo B in patients with very**
09:01:04 13 **high triglycerides based on Grimsgaard and Kurabayashi?**

09:01:09 14 A **No.**

09:01:09 15 Q **I'm sorry, I'm just asking you if you recall. You said**
09:01:12 16 **no?**

09:01:12 17 A **I'm sorry.**

09:01:13 18 Q **Let me read --**

09:01:14 19 **THE COURT: It's all right if you don't recall.**

09:01:17 20 **THE WITNESS: No, I do.**

09:01:19 21 **MR. ELIKAN: If you don't recall --**

09:01:18 22 **THE WITNESS: Please repeat the question.**

09:01:18 23 **MR. ELIKAN: I will.**

09:01:18 24 **BY MR. ELIKAN:**

09:01:20 25 Q **Do you recall that Dr. Heinecke testified that a person**

09:01:22 1 **of ordinary skill in the art would have reasonably expected**
09:01:27 2 **that 4 grams EPA would reduce apo B in patients with very high**
09:01:32 3 **triglycerides based on Grimsgaard, Nozaki, and Kurabayashi?**

09:01:38 4 A **Yes.**

09:01:39 5 Q **Did any of those references report reductions in apo B --**

09:01:44 6 A **No.**

09:01:45 7 Q **-- in patients -- hold on, Doctor.**

09:01:47 8 **Did any of those references report mechanism --**

09:01:52 9 **report reductions in apo B in patients with very high**

09:01:56 10 **triglycerides?**

09:01:57 11 A **No.**

09:01:58 12 Q **Would the person of ordinary skill in the art have looked**
09:02:03 13 **to those references in forming an expectation about the effect**
09:02:06 14 **of EPA on apo B in patients with very high triglycerides?**

09:02:12 15 A **No.**

09:02:13 16 Q **Why not?**

09:02:15 17 A **Because they didn't look at apo B in patients with very**
09:02:20 18 **high triglycerides.**

09:02:21 19 Q **Did Dr. Heinecke cite a single prior art reference**
09:02:25 20 **reporting that any omega-3 fatty acid formulation reduced apo**
09:02:34 21 **B in patients with very high triglycerides?**

09:02:37 22 A **No.**

09:02:37 23 Q **Beyond apo B some of the other asserted claims have**
09:02:40 24 **limitations that do not appear in claim 1 of the '782 patent.**
09:02:45 25 **I want to go through those now.**

09:02:46 1 Claim 1 the '728 patent claims a dose of about 4
09:02:51 2 grams of EPA a day, whereas claims 4 and 17 of the '560 patent
09:02:56 3 cover a daily dose of about 3.6 to 4 grams per day.

09:03:02 4 Do you have a different opinion or different
09:03:04 5 reasoning about the nonobviousness of those claims that have a
09:03:09 6 slightly different dose limitation or do you believe that the
09:03:12 7 same opinion and reasoning applies with equal force to those
09:03:16 8 claims?

09:03:17 9 A I believe the latter.

09:03:19 10 Q And turning to concurrent lipid altering therapy.

09:03:28 11 Whereas claim 1 of the '782 patent specifies that
09:03:32 12 the EPA is administered without concurrent lipid altering
09:03:37 13 therapy, other claims are silent on whether the subject
09:03:41 14 receives concurrent lipid altering therapy.

09:03:45 15 Do you have a different opinion or different
09:03:47 16 reasoning about the nonobviousness of those claims that are
09:03:51 17 silent on whether the subject is on concurrent lipid altering
09:03:55 18 therapy, or do you believe the same opinion and reasoning
09:03:58 19 applies with equal force to those claims?

09:04:01 20 A I believe the latter.

09:04:02 21 Q Some of the claims use different language than claim 1 of
09:04:09 22 the '782 patent to describe the effects of administering
09:04:12 23 Vascepa on LDL-C levels. I want to walk through that now.

09:04:17 24 MR. ELIKAN: Can we have PDX 6-36.
09:04:17 25

09:04:17 1 BY MR. ELIKAN:

09:04:20 2 Q And can you walk us through the claims and limitations.

09:04:24 3 A These are variations on LDL-C limitation in claims other
09:04:29 4 than claim 1 of the '728 patent.

09:04:31 5 Claim 1 of the '677 patent states "without
09:04:36 6 substantially increasing LDL-C compared to placebo control."

09:04:40 7 Claim 14 of the '715 patent states "without
09:04:45 8 effecting a statistically significant increase of [LDL-C] in
09:04:50 9 the subject."

09:04:51 10 Claims 4 and 17 of the '560 patent state "without
09:04:56 11 increasing LDL-C by more than 5 percent in the subject," and
09:05:01 12 "without increasing LDL-C in the subject compared to placebo
09:05:05 13 control."

09:05:05 14 And claim 1 of the '652 patent stating "without
09:05:10 15 substantially increasing LDL-C compared to baseline."

09:05:16 16 Q And as to those claims, do you have a different opinion
09:05:19 17 or different reasoning about their nonobviousness, or do you
09:05:24 18 believe the same opinion and reasoning applies with equal
09:05:28 19 force to those claims?

09:05:31 20 A The latter.

09:05:32 21 Q Let's talk about the two asserted claims that don't
09:05:37 22 mention LDL-C, claims 1 and 5 of the '929 patent.

09:05:41 23 MR. ELIKAN: Can we pull up PDX 6-37.

09:05:41 24 BY MR. ELIKAN:

09:05:46 25 Q Do you have a different opinion or different reasoning

09:05:50 1 about the nonobviousness of these two claims, claim 1 of the
09:05:55 2 '929 patent and 5 of the '929 patent, or do you believe the
09:06:01 3 same opinion and reasoning applies with equal force to these
09:06:05 4 claims?

09:06:05 5 A The latter.

09:06:07 6 Q In sum, then, what's your opinion on whether any of the
09:06:10 7 asserted claims would have been obvious?

09:06:13 8 A None of them would have been obvious.

09:06:16 9 MR. ELIKAN: Your Honor, can you give me one
09:06:19 10 moment?

09:06:19 11 THE COURT: Yes.

09:06:35 12 MR. ELIKAN: Your Honor, I have no further
09:06:36 13 questions at this time.

09:06:37 14 We have a technical issue. The screens at
09:06:42 15 counsel table, at least on our side, are not working. I don't
09:06:46 16 know whether you're experiencing --

09:06:48 17 MR. KLEIN: Ours are okay.

09:06:50 18 MR. ELIKAN: Yours are okay? Ours are not.

09:06:53 19 MR. SIPES: We're hoping when we flip over the
09:06:56 20 screens will come back. That's it.

09:06:58 21 THE COURT: Why don't we see if we can address
09:07:00 22 that issue before cross-examination, maybe, perhaps.

09:07:04 23 THE CLERK: I just flipped it over. Did it
09:07:07 24 change?

09:07:07 25 MR. SIPES: It did change.

09:07:09 1 THE CLERK: Is it coming up on all of the
09:07:11 2 **screens?**

09:07:12 3 MR. SIPES: Now it is.

09:07:13 4 THE COURT: Okay.

09:07:14 5 MR. ELIKAN: Thank you very much.

09:07:54 6 MR. KLEIN: May I proceed?

09:07:55 7 THE COURT: Yes.

09:07:57 8 MR. KLEIN: Good morning, Dr. Toth.

09:08:00 9 THE WITNESS: Good morning, Mr. Klein. Good to
09:08:02 10 see you again.

09:08:03 11 MR. KLEIN: You and I met at your deposition,
09:08:03 12 right?

09:08:06 13 THE WITNESS: Yes, we did.

09:08:06 14 MR. KLEIN: For the record, I'm Charles Klein.

09:08:08 15 I'll be asking you questions for the defendants.

09:08:10 16 Mr. Gross, can you put on DDX 10.1, please.

09:08:10 17 CROSS-EXAMINATION

09:08:10 18 BY MR. KLEIN:

09:08:20 19 Q Dr. Toth, were you here for Dr. Heinecke's direct?

09:08:23 20 A I was not present for it, no.

09:08:25 21 Q Okay. Did you read his testimony?

09:08:29 22 A Yes.

09:08:29 23 Q Okay. This -- I will represent to you that this slide

09:08:34 24 was used during Dr. Heinecke's direct. It was DX 6.75. Have

09:08:42 25 you seen this slide before?

09:08:44 1 A I don't believe I've seen the slide. I read the
09:08:50 2 **testimony.**

09:08:50 3 Q Okay. Why don't you take ten seconds, read through the
09:08:53 4 **slide to yourself, and let me know when you're done.**

09:08:57 5 A **(Witness reviews document.)**

09:09:00 6 Thank you.

09:09:02 7 Q Okay. Now, you understand the simple logic -- I know you
09:09:08 8 **disagree with it, but you understand the logic of defendants'**
09:09:13 9 **obviousness theory, right?**

09:09:15 10 A Yes.

09:09:15 11 Q Okay. And let's walk through this slide.

09:09:18 12 You agree that FDA approved Lovaza as a 4-gram per
09:09:23 13 day mixture of EPA and DHA for the claimed method of treating
09:09:28 14 patients with triglycerides over 500, correct?

09:09:30 15 A But increased LDL-C, yes.

09:09:39 16 Q Okay. It's important for you to listen to the question
09:09:41 17 and we'll take it one step at a time. I promise I will get to
09:09:46 18 the LDL-C issue.

09:09:48 19 Okay. Let me repeat the question. You agree that
09:09:50 20 FDA approved Lovaza as a 4-gram per day mixture of EPA and DHA
09:09:55 21 for the claimed method of treating patients with triglycerides
09:09:58 22 over 500, right?

09:09:59 23 A Yes.

09:09:59 24 Q Okay. And Lovaza has two active ingredients, EPA and
09:10:06 25 DHA, right?

09:10:06 1 A No, it is a mixture of omega-3 acid ethyl esters. There
09:10:12 2 are contaminants. It's not just a mixture of two things.
09:10:16 3 Q But the two active ingredients are EPA and DHA in Lovaza,
09:10:21 4 correct?
09:10:21 5 A No, it's organic acid ethyl esters.
09:10:24 6 Q Okay. Now, Doctor, purified EPA and purified DHA were
09:10:30 7 both known in the art as of March 2008, right?
09:10:33 8 A Yes.
09:10:33 9 Q And a POSA at that time who have understand that both DHA
09:10:41 10 and EPA were active components that lowered triglycerides,
09:10:45 11 right?
09:10:45 12 A Yes, they would have been active components that lower
09:10:49 13 triglycerides.
09:10:49 14 Q Okay. And Lovaza reported a side effect of increased
09:10:53 15 LDL-C, correct?
09:10:54 16 A Yes.
09:10:55 17 Q And, in your opinion, the LDL-C increases with Lovaza was
09:11:00 18 an important problem warranting new solutions, right?
09:11:03 19 A Yes.
09:11:04 20 Q You spent a lot of time on direct talking about that,
09:11:07 21 right?
09:11:07 22 A Sure did.
09:11:08 23 Q And it would have been obvious for a skilled artisan to
09:11:13 24 consider whether it was only one of Lovaza's agreement --
09:11:17 25 ingredients, the DHA or the EPA, for example, that causes the

09:11:22 1 **LDL side effect, correct?**

09:11:24 2 A **Not in patients with severe hypertriglyceridemia.**

09:11:27 3 Q **Okay. Now, I want to separate for a moment the question
of reasonable expectation of success, okay? Because -- and
we'll get to that.**

09:11:37 6 **But just looking at the Lovaza label, a skilled
artisan seeing that there's DHA and EPA in Lovaza, and seeing
a side effect, would at least consider whether the side effect
could be associated with only DHA or only EPA, correct?**

09:11:54 10 A **They could.**

09:11:56 11 Q **Okay. And because, after all, if that's true, if the
side effects associated with only DHA, for example, pure EPA
was known, and it could help those patients reduce
triglycerides without the side effect, right?**

09:12:14 15 A **Say that again, counsel?**

09:12:16 16 Q **Okay. If it turned out -- and we'll get to reasonable
expectation of success -- but a skilled artisan looking at the
Lovaza label could appreciate that if it turned out that the
side effect were attributed solely to DHA, it could -- the
skilled artisan would understand that using pure EPA could
benefit those patients who received the LDL-C side effect,
correct?**

09:12:42 23 A **But a skilled artisan wouldn't want to remove the DHA
given the benefits that it also appeared to occur.**

09:12:46 24 Q **Okay. Okay. But a skilled artisan would understand that**

09:12:54 1 pure EPA was available in the art, and if a patient had LDL-C
09:12:59 2 spikes with Lovaza and it was harmful, a skilled artisan would
09:13:04 3 appreciate that if EPA were LDL neutral, that could benefit
09:13:09 4 the patient, correct?
09:13:10 5 A But they had no reason to believe it was LDL neutral.
09:13:14 6 Q I get that, and I promise you we will get to that.
09:13:18 7 Now, you agree that Mori involved a study with 4
09:13:26 8 grams pure EPA and 4 grams per DHA, correct?
09:13:29 9 A Yes, it did.
09:13:30 10 Q And Mori found that LDL-C increased significantly with
09:13:34 11 DHA but not with EPA in the studied population, correct?
09:13:39 12 A Do I agree with that?
09:13:42 13 Q Well, that's what Mori found.
09:13:44 14 A Well, okay. Both groups increased.
09:13:47 15 THE COURT: I'm sorry, what was the answer?
09:13:49 16 THE WITNESS: Both groups increased numerically.
09:13:52 17 BY MR. KLEIN:
09:13:53 18 Q Okay. But Mori found that the increase of LDL-C with DHA
09:13:57 19 was statistically significant and the increase with EPA was
09:14:00 20 not, correct?
09:14:01 21 A Yes. But there was an imbalance on the baseline
09:14:05 22 triglyceride.
09:14:06 23 Q And we'll get to that. But that's what Mori reported,
09:14:09 24 correct?
09:14:09 25 A Yes.

09:14:09 1 Q Okay. And in view of Mori, it was at least obvious to
09:14:13 2 use 4 grams of purified EPA in patients with very high
09:14:17 3 triglycerides to try to avoid the LDL-C side effect of Lovaza,
09:14:22 4 correct?

09:14:22 5 A No.

09:14:24 6 Q Okay.

09:14:24 7 A They had no data on very high triglycerides. It was not
09:14:28 8 obvious.

09:14:28 9 Q All right. So this -- your answer is getting to the
09:14:32 10 issue of reasonable expectation of success, right?

09:14:35 11 A Yes.

09:14:35 12 Q Okay. And if I understand your opinion, you're saying a
09:14:40 13 skilled artisan would not do what I just asked because the
09:14:45 14 skilled artisan would not have a reasonable expectation of
09:14:48 15 success for two reasons, first, there's no LDL-C data in the
09:14:54 16 prior art for patients with very high triglycerides, and,
09:14:57 17 second, the skilled artisan would know that LDL-C goes up with
09:15:02 18 fibrates and Lovaza in that patient population; is that fair?

09:15:06 19 A And with niacin, any drug that had been tested to that
09:15:11 20 point led to an increase in LDL cholesterol because of
09:15:16 21 increased conversion of the VLDL to LDL in the patients with
09:15:23 22 very high triglycerides.

09:15:24 23 Q Okay. And we'll come back to that in a moment.

09:15:26 24 But your opinion with regard to reasonable
09:15:28 25 expectation of success really falls into two points, the lack

09:15:32 1 of data in the prior art and the references to Lovaza and
09:15:38 2 fibrates and niacin, right?

09:15:39 3 A There was remarkable consistency in the response, yes.

09:15:42 4 Q Okay. I want to focus on the first point, the lack of
09:15:46 5 LDL-C data.

09:15:47 6 Now, on direct you emphasize that there's LDL-C data
09:15:52 7 in the prior art for patients above 500 who were taking pure
09:15:58 8 EPA, right?

09:15:58 9 A Yes.

09:15:58 10 Q Okay. And you mention -- you talked about the Friedewald
09:16:01 11 equation, right?

09:16:02 12 A Yes, counsel.

09:16:03 13 Q And, in your opinion, a skilled artisan could not
09:16:05 14 reasonably expect pure EPA to have an LDL-C neutral effect in
09:16:10 15 patients with very high triglycerides because there's no
09:16:13 16 clinical data on that point, right?

09:16:16 17 A And because of the history of the use of other agents,
09:16:22 18 including EPA, DHA, and how patients respond, yes.

09:16:26 19 Q Okay. And for now, we'll get to that, but I want to
09:16:29 20 focus on the lack of data first.

09:16:31 21 In your opinion, prior art showing a neutral LDL-C
09:16:35 22 effect with pure EPA in patients below 500 won't translate
09:16:41 23 above 500, right?

09:16:42 24 A Well, but we never established that there was neutral
09:16:45 25 effect because we saw that there was inconsistency in the

09:16:48 1 results with EPA.

09:16:50 2 Q Okay. But, in your opinion, even if a skilled artisan
09:16:53 3 were looking at Mori which said there was no statistically
09:16:57 4 significant increase in LDL-C with pure EPA, your opinion is
09:17:01 5 that finding wouldn't translate above 500 without data,
09:17:05 6 correct?

09:17:06 7 A Correct.

09:17:07 8 Q Okay. And, in your opinion, a skilled artisan could not
09:17:11 9 know if 4 grams of pure EPA is LDL neutral until the
09:17:16 10 conclusion of a new clinical trial, correct?

09:17:19 11 A Well, that would most certainly be true, yes.

09:17:22 12 Q Okay. And even then, you would want to look at median
09:17:26 13 data in the clinical trial to assess whether the drug was LDL
09:17:31 14 neutral, right?

09:17:32 15 A Yes. You would want as much information as possible.

09:17:35 16 Q Okay. And anything short of a clinical study like that,
09:17:39 17 in your view, would not provide a reasonable expectation of
09:17:42 18 success. Is that your opinion?

09:17:43 19 A I'm sorry, counsel, repeat it, please.

09:17:46 20 Q Sure. Anything short of a new clinical trial in patients
09:17:50 21 with triglycerides above 500 showing LDL neutrality would be
09:17:56 22 insufficient to provide a reasonable expectation that you will
09:17:59 23 achieve that result, right?

09:18:01 24 A You would want a well done study to show this, yes.

09:18:04 25 Q Okay. And in your view, even if a skilled artisan were

09:18:09 1 to start testing 4 grams of pure EPA in patients with very
09:18:13 2 high triglycerides, in your view, there still would not be a
09:18:17 3 reasonable expectation of success until the results come out,
09:18:21 4 right?

09:18:21 5 A That's right.

09:18:22 6 Q And even if a skilled artisan came up with a clinical
09:18:30 7 trial protocol that said we're going to use 4 grams pure EPA
09:18:34 8 in patients with triglycerides above 500, and we're hoping
09:18:37 9 that it will be LDL neutral, that would not provide a
09:18:40 10 reasonable expectation of success in your view, right?

09:18:43 11 A No, because there was no foundation for thinking that it
09:18:46 12 would be neutral.

09:18:47 13 Q Okay. And certainly in your view, if a skilled artisan
09:18:51 14 simply reviewed the prior art and came up with a prediction
09:18:55 15 that LDL-C -- that pure EPA would be LDL-C neutral in patients
09:19:00 16 above 500, that would not be reasonable, a reasonable
09:19:05 17 prediction of success in your view, correct?

09:19:08 18 A It would not settle the issue.

09:19:10 19 Q Okay. And that's why in your view, the MARINE study
09:19:13 20 constituted an unexpected result; is that right?

09:19:16 21 A Yes.

09:19:16 22 Q Okay. And in your view, no skilled artisan could have
09:19:20 23 expected that 4 grams of pure EPA would be LDL-C neutral until
09:19:25 24 the MARINE study results came out, right?

09:19:28 25 A You would need a large enough study that was powered

09:19:33 1 **adequately to show neutrality.**

09:19:36 2 Q Okay. And you know the MARINE study results were not
09:19:40 3 known until late 2010?

09:19:42 4 A Yes.

09:19:45 5 Q And so in your view no one was able to reasonably expect
09:19:49 6 the LDL-C neutral effects seen in MARINE until late 2010,
09:19:54 7 correct?

09:19:54 8 A Not until the study was completed.

09:19:54 9 MR. KLEIN: Can we go to DDX 10.119.

09:19:54 10 BY MR. KLEIN:

09:20:03 11 Q Now, Doctor, on the screen is DX 1500. Do you recognize
09:20:10 12 this as the '728 patent?

09:20:10 13 A Yes.

09:20:11 14 Q Okay. Do you understand that Amarin filed its patent
09:20:11 15 applications in February 2009?

09:20:14 16 A Yes.

09:20:14 17 Q Okay. So Amarin applied for patents at least
09:20:19 18 one-and-a-half years before the MARINE study results came out,
09:20:22 19 right?

09:20:22 20 A Yes.

09:20:23 21 Q And you've read the patent, right?

09:20:25 22 A Yes.

09:20:25 23 MR. KLEIN: Let's go to DDX 10.120.

09:20:25 24 BY MR. KLEIN:

09:20:34 25 Q And, by the way, you understand that the patent

09:20:37 1 **specifications are identical for all the asserted patents?**

09:20:42 2 A **Yes.**

09:20:42 3 Q **Okay. So I'm just going to use the '728 patent as an example. Is that okay?**

09:20:46 5 A **Yes.**

09:20:46 6 Q **Now, on the screen is DX 1500, pages 14 and 16, and I'm focusing on column 2, lines 55 to 59, and column 5, lines 37 to 46.**

09:21:01 9 **And here you can see the patent says,**

09:21:05 10 **"In another embodiment, the subject or subject group being treated has a baseline triglyceride level of" -- and I'm just going to read the highlighting -- "at least about 500 milligrams per deciliter."**

09:21:18 15 **And then you can see later on it talks about all kinds of possible effects, and one of them is no increase in LDL-C levels. Do you see that?**

09:21:26 18 A **Yes.**

09:21:27 19 Q **Okay. Do you understand that this is all the patent says about using 4 grams pure EPA to treat very high triglycerides with no LDL-C effects?**

09:21:39 22 **MR. ELIKAN: Objection, Your Honor. This is well outside the scope of the direct. It also relates to the 112 issues that have been disposed of during the course of summary judgment practice.**

09:21:50 1 MR. KLEIN: Your Honor, this is highly relevant
09:21:52 2 to obviousness, and I'll cite three federal circuit cases that
09:21:56 3 I think Your Honor will find not only very interesting, but we
09:22:00 4 believe could be case dispositive.

09:22:02 5 I'll start with *Merck v Teva*, 395 F.3d 1364, pin
09:22:09 6 cite 1374, Federal Circuit 2005, reversing a nonobviousness
09:22:16 7 holding.

09:22:16 8 As well as *Alcon Research versus Apotex*, 687
09:22:22 9 F.3d 1362, pin cite 1369, Federal Circuit 2012.

09:22:29 10 And also *Hoffman Le Roche versus Apotex*, 748
09:22:34 11 F.3d 1326, pin cite 1331, Federal Circuit 2014.

09:22:40 12 These are all obviousness cases. I would prefer
09:22:43 13 not to discuss the holdings of those cases during my
09:22:47 14 cross-examination, but we will obviously brief this in
09:22:51 15 post-trial briefing and it relates to obviousness.

09:22:53 16 THE COURT: Mr. Elikan?

09:22:57 17 MR. ELIKAN: I have not actually read all of
09:22:59 18 these cases after hearing Mr. Klein's reference them. We're
09:23:03 19 happy to brief the issue. But if the -- it seems to me like
09:23:06 20 if he's -- if Mr. Klein believes that that opens the door to
09:23:10 21 this line of questioning, then we ought to be able to review
09:23:14 22 the cases and respond substantively.

09:23:17 23 He hasn't even mentioned what the holdings are.
09:23:20 24 We haven't had a chance to review them. I would suggest that
09:23:23 25 we move on to other things, that will allow us later to look

09:23:26 1 at the cases, and Mr. Klein can raise this issue again.

09:23:30 2 THE COURT: I'm sorry. But your -- I just want
09:23:32 3 to make sure I understand the objection.

09:23:34 4 The objection is this issue is not -- has
09:23:40 5 already been resolved on summary judgment.

09:23:44 6 MR. ELIKAN: It appears to be related to 112
09:23:47 7 issues. This isn't even an asserted claim. I have no idea
09:23:51 8 how this relates to anything. I believe it's not one of the
09:23:54 9 asserted claims.

09:23:54 10 MR. KLEIN: This is --

09:23:56 11 MR. ELIKAN: What?

09:23:57 12 MR. KLEIN: That's not a claim, that's a
09:23:58 13 specification.

09:24:00 14 MR. ELIKAN: I'm sorry. Do you have a number?

09:24:01 15 Okay. In any event, then it certainly isn't one
09:24:05 16 of the asserted claims, it's just a passage in the
09:24:07 17 specification. It appears to relate to 112 issues.

09:24:11 18 He's mentioned three cases saying it has
09:24:13 19 something to do with obviousness. We haven't looked at the
09:24:16 20 cases, I haven't even heard from Mr. Klein what the holdings
09:24:20 21 are or how the court discussed the issue.

09:24:22 22 So I would suggest we move on, and that will
09:24:24 23 allow us time during the break to look at the three cases if
09:24:28 24 they're provided to us.

09:24:29 25 THE COURT: I'm going to overrule the objection.

09:24:31 1 I'm going to allow the testimony based on the representation
09:24:35 2 that Mr. Klein is moving into the issue of obviousness, and if
09:24:39 3 it turns out that the cases do not support his argument, I'll
09:24:43 4 just ignore the testimony.

09:24:44 5 For now I'm going to continue.

09:24:46 6 Mr. Klein?

09:24:47 7 MR. KLEIN: Thank you.

09:24:47 8 BY MR. KLEIN:

09:24:53 9 Q Dr. Toth, do you understand that the statements we read
09:24:57 10 from the '728 patent specification and similar statements is
09:25:01 11 all the patents have to say about using 4 grams of pure EPA to
09:25:05 12 treat very high triglycerides with no LDL-C effect?

09:25:09 13 A That this is all?

09:25:12 14 Q Yes.

09:25:13 15 A I'm just reading it through.

09:25:26 16 Well, I see it --

09:25:28 17 THE COURT: Hang on. To be fair, do you want to
09:25:30 18 look at the entire patent? Because the question is not just
09:25:33 19 what this paragraph says, but you're asking Dr. Toth to
09:25:37 20 represent that this represents the entire patent.

09:25:42 21 MR. KLEIN: Let me ask a different question that
09:25:44 22 I think won't require Dr. Toth to read through the entire
09:25:48 23 patent.

09:25:48 24 BY MR. KLEIN:

09:25:49 25 Q Now, Dr. Toth, can we agree if you read the patent from

09:25:52 1 top to bottom you're not going to see any clinical data in the
09:25:56 2 patent?

09:25:57 3 A May I see the patent?

09:26:02 4 MR. KLEIN: It should be in your binder. It's
09:26:06 5 DX 1500.

09:26:06 6 BY MR. KLEIN:

09:26:12 7 Q And, Doctor, if it's helpful you did answer this question
09:26:14 8 in the deposition.

09:26:17 9 A This question?

09:26:18 10 Q Yeah. If I could play it, it won't be impeachment but it
09:26:22 11 will help move things along.

09:26:24 12 THE COURT: Instead of playing it, do you have
09:26:26 13 the transcript and the testimony --

09:26:27 14 MR. KLEIN: Yes, the --

09:26:27 15 THE COURT: -- you can show that to Dr. Toth.

09:26:30 16 MR. KLEIN: Sure the transcript is page 354,
09:26:33 17 lines 10 through 18.

09:26:35 18 THE COURT: Do you have the transcript?

09:26:38 19 THE WITNESS: What would the number of that be?

09:26:40 20 MR. KLEIN: Page 354. Do you have the
09:26:42 21 deposition?

09:26:48 22 THE WITNESS: Which, PX or DX --

09:26:50 23 MR. KLEIN: No. It's not -- it should just be a
09:26:53 24 transcript.

09:26:55 25 THE WITNESS: That I don't believe I have up

09:26:57 1 **here.**

09:26:57 2 **MR. KLEIN:** Hold on.

09:27:11 3 I'll be able to give you my copy.

09:27:16 4 **May I approach?**

09:27:17 5 **THE COURT:** Yes.

09:27:29 6 **MR. KLEIN:** And, Dr. Toth, it was 354, lines 10

09:27:32 7 through 18.

09:27:34 8 **THE WITNESS:** (Witness reviews document.)

09:27:47 9 Okay, counsel.

09:27:47 10 **BY MR. KLEIN:**

09:27:49 11 Q Okay. Does that refresh your recollection as to whether
09:27:52 12 there is clinical data in the patent?

09:27:54 13 A Yes.

09:27:54 14 Q Okay. And what is your recollection? Was there any
09:27:58 15 clinical data in the patent?

09:28:00 16 A No.

09:28:00 17 Q Okay. And would -- would it surprise you to learn
09:28:04 18 there's no animal data or *in vitro* data in the patent either?

09:28:10 19 A Not based on what I'm seeing here, no.

09:28:13 20 Q Okay. And so there's literally no support in the patents
09:28:18 21 for the claim that 4 grams pure EPA will be LDL neutral or
09:28:24 22 reduce apo B. Is that your understanding?

09:28:27 23 **MR. ELIKAN:** Renew the objection. This appears
09:28:29 24 to also be straight about 112, not obviousness. I don't even
09:28:33 25 understand how this can possibly relate to that.

09:28:35 1 MR. KLEIN: Well, maybe -- Your Honor, I'm
09:28:38 2 representing that it's about obviousness. If you disagree,
09:28:41 3 then 112 is not -- you told us we couldn't present 112 at
09:28:46 4 trial, so I'm not presenting 112. I'm presenting an
09:28:48 5 obviousness argument relating to a reasonable expectation of
09:28:51 6 success.

09:28:52 7 THE COURT: The objection is overruled.

09:28:54 8 BY MR. KLEIN:

09:28:56 9 Q Okay. Let's go to DX 10.121.

09:29:03 10 Doctor, I will represent to you that on the left is
09:29:07 11 DX 1500, pages 14 and 16, which is the '728 patent
09:29:12 12 specification we were reviewing, and on the right is Table 2
09:29:16 13 from Mori 2000, which is DX 1538, page 4.

09:29:23 14 Now, you understand that the Mori 2000 reference
09:29:26 15 contains more information about LDL neutral effects from 4
09:29:32 16 grams pure EPA than Amarin's own patents, correct?

09:29:36 17 A There is information in Mori and there's apparently no
09:29:44 18 data in the patent.

09:29:45 19 Q Okay. And so to be clear, you're arguing that clinical
09:29:49 20 data is required for a reasonable expectation of success, even
09:29:53 21 though the patent itself contains no clinical data, correct?

09:29:57 22 A Well, as I said in my deposition, I'm sure they had
09:30:01 23 something, but I don't know what it was.

09:30:02 24 Q Yeah. And that's actually my next question. Under your
09:30:06 25 theory, Amarin had no invention as of 2009 when it filed its

09:30:11 1 **patent application, correct?**

09:30:14 2 A **Well, clearly, they were basing their conclusion on**
something.

09:30:20 4 Q **Now, Doctor, you're here to defend the validity of the**
patents-in-suit, right?

09:30:26 6 A **Yes.**

09:30:26 7 Q **And you don't know what the inventors had to support**
09:30:30 8 **their claims in 2009 that using 4 grams pure EPA in patients**
09:30:35 9 **above 500 would, in fact, have LDL neutral effects and reduce**
09:30:39 10 **apo B, correct?**

09:30:40 11 A **I don't have the data in front of me, no.**

09:30:43 12 Q **Now, let's go back to the second argument you made with**
09:30:54 13 **regard to reasonable expectation of success. That is when you**
09:30:58 14 **looked to Lovaza, fibrates, and niacin. Do you remember that?**

09:31:01 15 A **Yes.**

09:31:01 16 Q **Okay. And on direct you testified that a skilled artisan**
09:31:06 17 **would believe that both EPA and DHA raise LDL-C in patients**
09:31:11 18 **with very high triglycerides by looking to those three classes**
09:31:15 19 **of drugs, correct?**

09:31:16 20 A **Yes.**

09:31:17 21 Q **All right. And the fact that Lovaza itself has an LDL-C**
09:31:23 22 **side effect doesn't answer the question of whether that side**
09:31:26 23 **effect could be attributed to solely EPA or solely DHA,**
09:31:31 24 **correct?**

09:31:31 25 A **Yes, that's correct.**

09:31:32 1 Q Okay. So that's why you rely on niacin and the fibrates,
09:31:36 2 correct?

09:31:36 3 A Well, it's all of a piece.

09:31:39 4 Q Right.

09:31:41 5 Okay. Let's go to DDX 10.3.

09:31:53 6 Now, you understand that Amarin made this same
09:31:57 7 argument to the patent office?

09:31:58 8 A Which same argument?

09:32:00 9 Q The same argument with regard to fibrates.

09:32:04 10 A Please repeat what the argument is.

09:32:07 11 Q Okay. Well, we're actually looking at it. On the screen
09:32:10 12 is DX 1522, page 772, and this is Amarin's June 2011 response
09:32:19 13 to the patent office rejection.

09:32:22 14 And I won't read the whole thing, but I'll just read
09:32:25 15 what is essentially highlighted, which is,

09:32:27 16 "Amarin argued to the patent office that the
09:32:30 17 actual evidence of record indicates that any change
09:32:34 18 in LDL in those subjects is not at all predictive of
09:32:38 19 the impact on LDL in subjects with very high
09:32:42 20 triglycerides."

09:32:44 21 And then if you go to the subparagraphs,

09:32:46 22 "Amarin argued that approved medications for
09:32:50 23 triglyceride lowering in this very high triglyceride
09:32:53 24 patient population, e.g., Lovaza, Trilipix, Lopid, et
09:32:59 25 cetera, all increase LDL-C."

09:33:01 1 And if you go to the second indented
09:33:03 2 paragraph, "Amarin argued that subjects with very
09:33:06 3 high triglycerides clearly respond very differently
09:33:09 4 to triglyceride-lowering therapy compared to subjects
09:33:13 5 with borderline high, high triglyceride levels."

09:33:17 6 Do you understand that Amarin made those types
09:33:18 7 of arguments to the patent office?

09:33:20 8 A **Yes.**

09:33:20 9 Q Okay. And those are the same arguments that you made in
09:33:23 10 your direct testimony, correct?

09:33:24 11 A **Yes.**

09:33:25 12 Q And Trilipix and Lopid are fibrates, right?

09:33:32 13 A **Yes, they are.**

09:33:36 14 Q All right. Let's go to DDX 10.4, and this is DX 1587,
09:33:42 15 page 19.

09:33:42 16 And here the examiner responded and said,
09:33:48 17 "Triplix" -- I think that's a typo, it should be Trilipix.

09:33:55 18 "...which is a fenofibric acid, is
09:33:55 19 structurally and biologically very different from
09:33:59 20 EPA-E an omega-3 fatty acid."

09:34:02 21 And you skip a sentence, it says,
09:34:04 22 "On the other hand EpaDEL is omega-3 fatty
09:34:08 23 acid known to lower triglycerides although the
09:34:11 24 mechanism is not known," and the examiner said, "so
09:34:15 25 one cannot extrapolate the results observed with the

09:34:21 1 fibrate Trilipix to omega-3 fatty acids like EPA."

09:34:23 2 Were you aware that the examiner rejected

09:34:26 3 Amarin's argument that a skilled artisan would extrapolate the

09:34:26 4 results observed with a fibrate to omega-3 fatty acids like

09:34:31 5 pure EPA?

09:34:31 6 A Yes.

09:34:31 7 Q Okay. And on direct you extrapolated the results

09:34:37 8 observed with the fibrate to purified EPA, correct?

09:34:40 9 A Yes.

09:34:40 10 Q And so your position is the patent office got this point

09:34:45 11 wrong, right?

09:34:46 12 A Yes, that's correct, counsel.

09:34:48 13 Q And, by the way, on direct you discuss prior art talking

09:34:54 14 about how niacin, fibrates, and Lovaza can all increase LDL

09:34:58 15 when triglycerides get very high, right?

09:35:00 16 A Yes.

09:35:01 17 Q But you did not cite on direct any prior art comparing

09:35:04 18 the LDL-C effects of niacin or fibrates on the one hand with

09:35:09 19 pure EPA, correct?

09:35:11 20 A There wasn't any data to go on.

09:35:15 21 Q Let's go to slide DDX 10.5.

09:35:25 22 Doctor, you understand that during prosecution, the

09:35:30 23 patent office repeatedly rejected the patents as obvious,

09:35:35 24 right?

09:35:35 25 A Yes.

09:35:35 1 Q And in the Notice of Allowance the examiner wrote,
09:35:38 2 "Based on these references" -- referring to
09:35:40 3 prior art -- "it was concluded that it will be
09:35:43 4 obvious to treat patients having triglycerides above
09:35:47 5 500 milligrams with 96 percent pure ethyl EPA,"
09:35:51 6 right?

09:35:51 7 A Yes.

09:35:52 8 Q And the examiner ultimately issued the patent based on
09:35:57 9 those secondary considerations listed on the screen, and, for
09:36:02 10 the record, it's DX 1591, pages 5 and 6. Correct?

09:36:07 11 A Yes.

09:36:07 12 Q Now, you understand that the patent office thus found
09:36:10 13 that the prior art would have motivated a skilled artisan to
09:36:14 14 use purified EPA in patients with triglycerides above 500,
09:36:17 15 right?

09:36:17 16 A Counsel, say that again? I'm sorry.

09:36:19 17 Q You understand that the patent office found that the
09:36:23 18 prior art would have motivated a skilled artisan to use
09:36:28 19 purified EPA in patients above 500, correct?

09:36:31 20 A That was one point of contention.

09:36:33 21 Q Okay. But that's what the patent office found, right?

09:36:39 22 A Yes.

09:36:40 23 Q Okay. And you understand the patent office found a
09:36:44 24 reasonable expectation of success in using EPA to reduce
09:36:48 25 triglyceride levels below 500, right?

09:36:51 1 A Yes.

09:36:51 2 Q And you're offering testimony today on the point that the

09:36:56 3 Patent Office got that wrong, correct?

09:36:59 4 A Yes.

09:37:01 5 Q Now, I want to unpack your opinion with regard to

09:37:13 6 extrapolating to fibrates and niacin in a little more depth.

09:37:20 7 Am I correct that, in your opinion, a skilled

09:37:23 8 artisan would believe that when patients have triglycerides

09:37:26 9 above 500, the triglyceride level will necessarily increase --

09:37:34 10 the reduction of triglycerides will necessarily increase

09:37:37 11 LDL-C?

09:37:38 12 A Correct.

09:37:38 13 Q Okay. And, in your opinion, the higher the baseline

09:37:42 14 triglyceride level, the more likely you're going to see an

09:37:45 15 LDL-C increase?

09:37:46 16 A Yes.

09:37:47 17 Q And that -- and you point to Lovaza and fibrates and

09:37:51 18 niacin as an example, right?

09:37:52 19 A Yes.

09:37:53 20 Q And, in your view, a skilled artisan wouldn't think that

09:37:56 21 a drug could reduce triglycerides in patients with very high

09:38:01 22 triglyceride levels without also increasing LDL-C.

09:38:05 23 A Based on the prior art, yes.

09:38:07 24 Q Okay. And you said on direct something to effect that

09:38:09 25 all drugs approved for severe hypertriglyceridemia have a

09:38:14 1 common theme, LDL elevation is proportionate to the magnitude
09:38:20 2 of the baseline triglycerides, something like that; is that
09:38:22 3 right?

09:38:22 4 A Something like that, yes.

09:38:23 5 Q Okay. And that's what I wrote down so hopefully I got it
09:38:28 6 right.

09:38:28 7 And this is why, in your opinion, Vascepa had
09:38:31 8 unexpected results and satisfied a long-felt need, right?

09:38:34 9 A Yes.

09:38:37 10 Q Now, this is a critical point supporting your
09:38:40 11 nonobviousness opinion, you spent a lot of time on it, right?

09:38:43 12 A Yes.

09:38:44 13 Q Now, Doctor, it was known before 2008 that patients with
09:38:48 14 triglycerides above 500 could take a drug that both reduces
09:38:53 15 triglyceride levels and also reduces LDL-C.

09:38:57 16 A It was known?

09:39:00 17 Q It was known, right?

09:39:02 18 A Prior to --

09:39:04 19 Q March 2008.

09:39:08 20 A Well, the patent that was submitted by Amarin would
09:39:12 21 suggest that they knew something about it, but it was not
09:39:16 22 generally known, no.

09:39:19 23 Q Okay. Well, Vascepa was not the first FDA-approved
09:39:22 24 treatment shown to reduce triglycerides from above 500 to
09:39:26 25 below 500 without increasing LDL-C, right?

09:39:31 1 A No, I'm not aware of that.

09:39:34 2 Q Okay. Doctor, are you familiar with LIPITOR?

09:39:38 3 A Of course I'm familiar with LIPITOR, counsel.

09:39:40 4 Q You've prescribed is thousands of times, right?

09:39:43 5 A Yes, probably.

09:39:44 6 Q It's probably one the most prescribed drugs of all time,

09:39:48 7 right?

09:39:48 8 A Yes.

09:39:48 9 Q And LIPITOR was available before March 2008?

09:39:51 10 A Yes.

09:39:51 11 Q And a skilled artisan by March 2008 would be very

09:39:56 12 familiar with the LIPITOR label, right?

09:39:59 13 A They would.

09:39:59 14 Q Now, LIPITOR is primary used for cardiovascular risk

09:40:03 15 reduction, correct?

09:40:04 16 A Yes, counsel.

09:40:05 17 Q And LIPITOR is not specifically indicated to treat all

09:40:10 18 patients with severe hypertriglyceridemia, right?

09:40:11 19 A It had no indication to treat severe hypertriglyceridemia

09:40:15 20 at all.

09:40:15 21 Q Okay. But LIPITOR was and actually still is FDA approved

09:40:20 22 to reduce triglycerides in some patients who have levels above

09:40:25 23 500, right?

09:40:26 24 A It is -- okay. So -- may I see the label where it says

09:40:33 25 that?

09:40:34 1 MR. KLEIN: Yes, let's go to the label. Let's
09:40:36 2 go to DDX 10.6. And on the screen is DX 3007, page 14.
09:40:45 3 And there's a housekeeping issue here, Your
09:40:47 4 Honor, because the current LIPITOR label is in evidence as
09:40:52 5 DX 1986. DX 3007, which I'm using for impeachment is not
09:40:58 6 in -- on the exhibit list, but I'd like to use it because it's
09:41:02 7 dated before March 2008 and the relevant language is identical
09:41:06 8 to the LIPITOR exhibit that is in evidence, and so I move to
09:41:12 9 admit DX 3007.

09:41:15 10 THE COURT: So has the LIPITOR label changed?

09:41:18 11 MR. KLEIN: Not the portions I'm going to talk
09:41:19 12 about. But I would like to move into evidence DX 3007 solely
09:41:24 13 because this is the label that's dated before March 2008.

09:41:30 14 THE COURT: Any objection?

09:41:32 15 MR. ELIKAN: Yes, Your Honor. It's not on the
09:41:33 16 exhibit list, and they have another LIPITOR label on the
09:41:37 17 exhibit list.

09:41:38 18 I understand that they may want to use this for
09:41:40 19 impeachment, but I don't understand why it would be added now
09:41:44 20 to the exhibit list based on a representation made in court.

09:41:48 21 The deadline to put in exhibits was in early
09:41:52 22 January, weeks ago. I can understand using it for
09:41:55 23 impeachment. We have no objection to that but don't see why
09:41:58 24 it should be admitted into evidence.

09:42:00 25 MR. KLEIN: Your Honor, the local rules as well

09:42:02 1 as the pretrial order do not require documents to be used for
09:42:08 2 impeachment to be identified on the exhibit list, and it
09:42:12 3 doesn't preclude us from moving them into evidence, which is
09:42:15 4 what I'm doing.

09:42:16 5 And there's obviously no prejudice because the
09:42:19 6 only difference is that this makes it clear it was revised in
09:42:25 7 2007.

09:42:25 8 THE COURT: Well, there is such an exception to
09:42:30 9 the rule that allows for impeachment evidence not to be
09:42:32 10 disclosed before the impeachment, but what I'm understanding
09:42:37 11 is the portion that you're using to impeach is the same as
09:42:41 12 that on the exhibit that's already been admitted.

09:42:43 13 MR. KLEIN: Correct.

09:42:44 14 THE COURT: So, really, you're not using
09:42:46 15 anything new to impeach. You just want to have this label be
09:42:50 16 admitted because it's one that was in existence in 2007 to
09:42:55 17 make the record clear.

09:42:56 18 MR. KLEIN: Exactly.

09:42:57 19 THE COURT: So how can you use the exception to
09:42:59 20 try to get the evidence in when you're not really using it for
09:43:03 21 impeachment?

09:43:03 22 MR. KLEIN: Well, I am --

09:43:05 23 THE COURT: Well, in other words, what you need
09:43:06 24 for impeachment is already in the other exhibit.

09:43:10 25 MR. KLEIN: Well, this makes it very clear that

09:43:12 1 what's in the other exhibit was in the LIPITOR label as of
09:43:17 2 March 2008, and Dr. Toth said he wasn't aware of any drug that
09:43:22 3 was approved for patients above 500.

09:43:25 4 So it's being used for impeachment, and the only
09:43:27 5 reason I want it move this label in is to make the record
09:43:32 6 clear that this -- that the language was in the prior art.

09:43:38 7 THE COURT: Well, I understand why you want the
09:43:42 8 2007 label in, because we're looking at March -- at this point
09:43:48 9 anyway, the March 2008 as the time period.

09:43:53 10 I'm just pointing out that using the rule that
09:43:55 11 allows for impeachment evidence not to be disclosed prior to
09:43:59 12 the impeachment doesn't seem to fit here because what you --
09:44:02 13 the content of what you're using it to impeach is not in this
09:44:05 14 new exhibit.

09:44:06 15 Am I right?

09:44:07 16 MR. KLEIN: Yes, except part of the impeachment
09:44:10 17 is that this was in the prior art.

09:44:14 18 THE COURT: All right. Anymore comment before I
09:44:17 19 give my ruling? Mr. Elikan?

09:44:20 20 MR. ELIKAN: I mean --

09:44:20 21 THE COURT: The parties don't dispute that this
09:44:22 22 is in the prior art. There's no dispute that LIPITOR was in
09:44:26 23 existence before 2000 -- it's been around for a long time.

09:44:31 24 MR. ELIKAN: Your Honor, there should be --
09:44:33 25 there is a LIPITOR label that's on the exhibit list. My only

09:44:37 1 issue is moving this into evidence.

09:44:38 2 Simply, we're fine with it being used as
09:44:41 3 impeachment, but it seems that Mr. Klein then ought to be
09:44:45 4 comparing the two labels and showing that whatever he says is
09:44:48 5 in this older label is in the newer label.

09:44:52 6 We don't see how this is not having to disclose
09:44:55 7 impeachment evidence in advance translates to being able to
09:44:58 8 admit impeachment materials.

09:45:02 9 THE COURT: Mr. Klein?

09:45:03 10 MR. KLEIN: The -- the only issue for
09:45:06 11 impeachment is the date. The content is the same. I can
09:45:09 12 obviously go through this as impeachment and then go through
09:45:13 13 the current label and compare them, ask if they've changed.

09:45:16 14 But I don't think there's going to be a dispute,
09:45:19 15 and it seems like a waste of time when all we're disputing is
09:45:23 16 whether I could put into the evidence something to establish
09:45:25 17 that this was the language before March 2008.

09:45:27 18 THE COURT: All right. If you're not using
09:45:30 19 anything -- if you're saying that what you're using in this
09:45:32 20 label is the same material that's already in the label that's
09:45:35 21 admitted as 1986, Exhibit 1986?

09:45:41 22 MR. KLEIN: Correct.

09:45:41 23 THE COURT: I'm going to overrule the objection.
09:45:43 24 I'm going to admit DX 3007, the 2007 LIPITOR label, solely for
09:45:50 25 the limited purpose of establishing that the label was in

09:45:53 1 **existence in 2007.**

09:45:55 2 MR. KLEIN: Okay. Thank you.

09:45:55 3 (Defendants' Exhibit 3007 received in
09:45:58 evidence.)

09:45:58 4 **BY MR. KLEIN:**

09:45:58 5 Q Okay. Now, Doctor, to get back on track, we're looking
09:46:02 6 at DX 3007, page 14. You asked to look at the LIPITOR label.
09:46:07 7 Do you recognize DX 3007 as the LIPITOR label revised as of
09:46:13 8 September 2007?

09:46:14 9 A Yes, I recognize it.

09:46:16 10 Q Okay. And it says "LIPITOR is indicated" -- and you go
09:46:19 11 to number two.

09:46:20 12 "...as an adjunct to diet for the treatment
09:46:23 13 of patients with elevated serum triglyceride levels,
09:46:27 14 Frederickson Type IV."

09:46:29 15 Do you see that?

09:46:30 16 A Yes.

09:46:30 17 Q And Frederickson Type IV includes some patients with
09:46:33 18 triglycerides above 500, right?

09:46:36 19 A Very few. Fredrickson Type IV is typically less than
09:46:40 20 500, typically between 350 and 499, and this was also
09:46:44 21 indicated in the Tricor label.

09:46:46 22 MR. KLEIN: Okay. Let's go to DDX 10.7.

09:46:46 23 **BY MR. KLEIN:**

09:46:51 24 Q Okay. I added the relevant portion of the label with
09:46:54 25 regard to Fredrickson Type IV hypertriglyceridemia, and this

09:46:59 1 section talks about how the response to LIPITOR in 64 patients
09:47:03 2 with isolated hypertriglyceridemia were treated across several
09:47:09 3 clinical trials as shown in a table below, and the median
09:47:13 4 baseline -- median baseline triglyceride level was 565. Do
09:47:19 5 you see that?

09:47:20 6 A Yes.

09:47:21 7 MR. ELIKAN: Your Honor --

09:47:21 8 THE COURT: There's an objection?

09:47:22 9 MR. ELIKAN: Yes. He should at least be
09:47:24 10 provided with the label. I don't think he has that now.

09:47:26 11 If he's being shown other portions of it, he has
09:47:29 12 a different version as I understand it, we certainly don't.

09:47:33 13 MR. KLEIN: No -- I think you do.

09:47:35 14 MR. ELIKAN: I don't believe so.

09:47:37 15 MR. KLEIN: You should.

09:47:37 16 BY MR. KLEIN:

09:47:38 17 Q Doctor, do you have DX 3007 in your binder?

09:47:46 18 THE COURT: So I admitted DX 3007 solely to show
09:47:51 19 that the label was in existence in 2007 based on your
09:47:57 20 representation, Mr. Klein, that the portion you were asking is
09:47:59 21 the same in both labels.

09:48:01 22 I know that you prepared this already so you're
09:48:03 23 referencing 3007, and I'm allowing you to proceed based on the
09:48:08 24 representation that the materials in both 3007 and 1986 are
09:48:13 25 the same.

09:48:14 1 MR. KLEIN: Yes. Right. Yes, Your Honor.

09:48:17 2 May Ms. Heydorn approach the witness?

09:48:31 3 THE COURT: Yes.

09:48:31 4 THE WITNESS: Thank you.

09:48:32 5 BY MR. KLEIN:

09:48:33 6 Q Now, Doctor, you can see this is referring to pages 11
09:48:37 7 and 14. If you need to look at the document, can you look at
09:48:40 8 the document. But, you can see that the baseline triglyceride
09:48:43 9 level on the LIPITOR label for the hypertriglyceridemia
09:48:50 10 section was 565, right?

09:48:51 11 A Yes.

09:48:51 12 Q And, okay, a patient with triglyceride levels of 565 is
09:48:56 13 obviously above 500?

09:48:58 14 A If a patient has a 565, it's over 500.

09:49:01 15 Q Okay. And more importantly that patient has severe
09:49:05 16 hypertriglyceridemia?

09:49:05 17 A Yes, but it doesn't say how many patients here had severe
09:49:10 18 hypertriglyceridemia.

09:49:10 19 Q Okay. Well, let's go -- look at DDX 10.8.

09:49:18 20 A Counsel, which page is that going to be on?

09:49:22 21 Q It's on 11 and 12.

09:49:24 22 A Okay.

09:49:25 23 Q And this is Table 4.

09:49:32 24 A This is still the LIPITOR label?

09:49:37 25 Q Correct.

09:49:38 1 A It says DX 1966.

09:49:41 2 MR. KLEIN: Maybe you're on the --

09:49:43 3 THE COURT: That's not the correct exhibit.

09:49:44 4 MR. KLEIN: It should be DX 3007.

09:49:47 5 THE WITNESS: Okay. Page 11, you said?

09:49:50 6 MR. KLEIN: Eleven and 12.

09:49:53 7 THE WITNESS: I have it.

09:49:54 8 MR. KLEIN: Okay. And I'm just going to look at

09:49:56 9 it focus on the table. I'm not sure there's anything else you

09:49:59 10 need but you're welcome to look at the exhibit if you want.

09:49:59 11 BY MR. KLEIN:

09:50:04 12 Q The generic name for LIPITOR is Atorvastatin, right?

09:50:11 13 A Yes.

09:50:11 14 Q Okay. So this Table 4 compares LIPITOR 10 milligrams,

09:50:15 15 20 milligrams, and 80 milligrams to a placebo, right?

09:50:19 16 A Yes.

09:50:19 17 Q Okay. And according to Table 4 from the 2007 LIPITOR

09:50:25 18 label, and I'll represent to you that this hasn't changed,

09:50:28 19 triglyceride levels were reduced 41 percent with 10 milligrams

09:50:34 20 of LIPITOR, right?

09:50:36 21 A Yes.

09:50:36 22 Q And LDL-C went down 26.5 percent, right?

09:50:40 23 A Yes.

09:50:41 24 Q And for 20 milligrams, it was similar, triglycerides went

09:50:47 25 down 39 percent, right?

09:50:49 1 A Yes.

09:50:50 2 Q And LDL-C went down 30.4 percent, right?

09:50:55 3 A Yes.

09:50:55 4 Q And for 80 milligrams, triglycerides went down

09:50:59 5 52 percent, right?

09:50:59 6 A Yes.

09:51:00 7 Q And LDL-C went down 40.5 percent.

09:51:04 8 A Yes.

09:51:05 9 MR. KLEIN: Now, let's go to DDX 10.9.

09:51:05 10 BY MR. KLEIN:

09:51:11 11 Q Okay. On the left, we've got the portions of the LIPITOR

09:51:16 12 label we were looking at, DX 3007, page 12. And on the right

09:51:21 13 we have the Lovaza PDR, DX 1535, page 3.

09:51:26 14 Do you see that?

09:51:28 15 A Yes.

09:51:28 16 Q And you rely on Table 2 from the Lovaza label to show

09:51:33 17 that LDL-C went up 49.3 percent, right?

09:51:36 18 A Yes.

09:51:37 19 Q Now, the median baseline triglycerides reported in the

09:51:42 20 Lovaza PDR were 816, right?

09:51:46 21 A Yes.

09:51:46 22 Q And in contrast, the median baseline triglyceride level

09:51:50 23 in the LIPITOR label was 565, right?

09:51:55 24 A Yes. The distinction I would draw here is that everybody

09:51:58 25 in the Lovaza study had triglycerides over 500. We have no

09:52:02 1 idea how many in the LIPITOR study did.

09:52:05 2 Q Okay. But we do know the median triglyceride level was

09:52:09 3 above 500, right?

09:52:10 4 A I don't find that helpful.

09:52:12 5 Q Okay. You don't find median data helpful?

09:52:17 6 A Well, I need to know how many patients were above and

09:52:20 7 below 500, and what happened above and below 500.

09:52:24 8 Q Okay. Now, you testified that the higher the

09:52:27 9 triglyceride baseline, the more likely you are to have an

09:52:32 10 LDL-C increase, right?

09:52:33 11 A Yes.

09:52:33 12 Q And a skilled artisan would know that, that's your

09:52:37 13 opinion?

09:52:37 14 A Hopefully, yes.

09:52:39 15 Q So a skilled artisan would expect different LDL-C effects

09:52:43 16 from a drug treating a patient with a baseline triglyceride

09:52:46 17 level of 500, as opposed to a patient with a triglyceride

09:52:50 18 level above 800, correct?

09:52:53 19 A Yes.

09:52:54 20 Q Okay. And you understand every asserted claim in this

09:53:00 21 case covers patients with triglyceride levels of 500 and

09:53:04 22 above, right?

09:53:05 23 A And above, yes.

09:53:06 24 Q Okay. But it includes patients who have a triglyceride

09:53:10 25 level of only 500?

09:53:11 1 A Sure. Greater than or equal to 500.

09:53:19 2 Q And so you understand that if it were obvious to use

09:53:22 3 4 grams pure EPA to get an LDL neutral effect in a patient

09:53:28 4 with triglyceride levels of exactly 500, those claim

09:53:32 5 limitations would be obvious, right?

09:53:34 6 A No. No, no.

09:53:39 7 Based on what?

09:53:40 8 Q You understand there's no such thing as "partial

09:53:43 9 obviousness" of a claim?

09:53:45 10 A Yes.

09:53:46 11 Q Okay. So if it's obvious to get an LDL neutral effect

09:53:50 12 with a patient at 500, you understand the claims are obvious,

09:53:54 13 right?

09:53:59 14 And if you don't understand, it's a legal question.

09:54:02 15 That's fine, too. I know it's a legal issue.

09:54:05 16 A Yeah. I must say I'm not familiar with that.

09:54:07 17 Q Okay. But no asserted patent in this case requires

09:54:13 18 triglyceride levels to be above 800, right?

09:54:15 19 A No. That's correct.

09:54:16 20 MR. KLEIN: Okay. Let's go to DDX 10.118.

09:54:16 21 BY MR. KLEIN:

09:54:23 22 Q This is PDX 6.7 that you used on direct. Do you remember

09:54:28 23 that?

09:54:28 24 A Yes.

09:54:28 25 Q Okay. And I want to focus on the high triglyceride bar

09:54:35 1 **you had there.**

09:54:36 2 A **Yes.**

09:54:36 3 Q **And just to orient everyone, this is for Tricor, right?**

09:54:44 4 A **Yes.**

09:54:44 5 Q **Okay. And this refers to triglycerides of 350 to 499,**
right?

09:54:49 7 A **Which was defined as Type IV, as Fredrickson's Type IVs,**
yes.

09:54:56 9 Q **And the mean was -- the mean triglyceride level was 432,**
right?

09:54:59 11 A **Yes.**

09:55:00 12 Q **And in this group there was no statistically significant**
increase in LDL-C, correct?

09:55:05 14 A **Yes.**

09:55:06 15 Q **And triglyceride levels of 499 and 500 are within error**
of the measurement, right?

09:55:17 17 A **That would be true.**

09:55:17 18 Q **Okay. And, again, the claims here start at 500, right?**

09:55:22 19 A **Yes.**

09:55:22 20 Q **And they --**

09:55:24 21 MR. KLEIN: **Can you cut out.**

09:55:24 22 BY MR. KLEIN:

09:55:26 23 Q **Your very high triglyceride bar has a mean of 726, right?**

09:55:31 24 A **Yes.**

09:55:32 25 Q **There's no claim in this case that requires triglycerides**

09:55:36 1 **above 700, right?**

09:55:37 2 A **Correct.**

09:55:46 3 MR. KLEIN: All right. Let's move to DDX 10.10.

09:55:46 4 **BY MR. KLEIN:**

09:55:51 5 Q And I'm hoping that we can move through these points

09:55:54 6 fairly quickly. You recognize DX 1635, page 3, as the Lovaza

09:56:01 7 PDR?

09:56:04 8 A Yes.

09:56:04 9 Q And the Lovaza indication is the same method covered by

09:56:08 10 the claims to treat adult patients with very high triglyceride

09:56:11 11 levels, right?

09:56:12 12 A Yes.

09:56:13 13 Q And as of March 2008, a skilled artisan would have found

09:56:17 14 it obvious to treat a patient with triglyceride levels above

09:56:21 15 500 with a 4-gram per day mixture of EPA and DHA according to

09:56:26 16 the Lovaza label, right?

09:56:28 17 A Well, defined as omega-3 acid ethyl esters, yes.

09:56:35 18 Q And the label discusses a clinical trial that lasted --

09:56:40 19 there are two clinical trials, but one of them lasted

09:56:43 20 16 weeks, right?

09:56:43 21 A Yes.

09:56:44 22 Q And so it would have been obvious to a skilled artisan,

09:56:47 23 as of March 2008, to treat patients with severe

09:56:50 24 hypertriglyceridemia for at least 12 weeks, that they

09:56:53 25 can be treated, right?

09:56:54 1 A Yes.

09:56:57 2 MR. KLEIN: Let's go to DDX 10.11.

09:56:57 3 BY MR. KLEIN:

09:57:02 4 Q This is DX 1535 page 3. We're still on the Lovaza PDR.

09:57:09 5 And I don't think there's going to be any dispute

09:57:12 6 here, but a side effect of Lovaza is LDL-C increase, right?

09:57:16 7 A Yes.

09:57:16 8 Q And in your opinion, as of March 2008, a skilled artisan

09:57:20 9 would have been motivated to avoid LDL-C increases when

09:57:24 10 treating patients with severe hypertriglyceridemia, right?

09:57:25 11 A Yes.

09:57:26 12 Q And as of March 2008, many patients who took Lovaza were

09:57:31 13 also given a statin to address the LDL-C increases, right?

09:57:35 14 A Yes.

09:57:35 15 Q And those patients would have to take two pills, the

09:57:39 16 Lovaza and a statin, right?

09:57:40 17 A Yes.

09:57:41 18 Q And as of March 2008, a skilled artisan would have been

09:57:45 19 motivated to develop a single pill that treats severe

09:57:50 20 hypertriglyceridemia without LDL-C increases, correct?

09:57:54 21 A Sure.

09:57:54 22 Q Now, the patent claims require purified EPA, right?

09:58:00 23 A Yes.

09:58:01 24 Q And the prior art taught that both EPA and DHA could be

09:58:06 25 purified, correct?

09:58:07 1 A Yes.

09:58:07 2 Q And you are aware of Epadel before March 2008, right?

09:58:11 3 A Yes.

09:58:12 4 Q Okay. And Epadel was approved in the 1990s; is that

09:58:17 5 right?

09:58:17 6 A Yes. In Japan.

09:58:19 7 MR. KLEIN: In Japan.

09:58:20 8 Let's go to DDX 10.12. This is DX 1528, page 3.

09:58:20 9 BY MR. KLEIN:

09:58:26 10 Q Do you recognize this as the Epadel PI?

09:58:31 11 A Yes, counsel.

09:58:32 12 Q Okay. And a skilled artisan would have been aware of

09:58:36 13 Epadel, at a minimum, because of the JELIS trial, right?

09:58:39 14 A Yes.

09:58:40 15 Q Okay. And the JELIS trial was not conducted by Amarin,

09:58:44 16 right?

09:58:44 17 A Correct.

09:58:44 18 Q And purified EPA, such as Epadel, was given to patients

09:58:50 19 before March 2008 to reduce triglyceride levels, right?

09:58:54 20 A Yes.

09:58:56 21 Q And a skilled artisan, as of March 2008, would have found

09:59:02 22 it obvious to use either pure DHA, or pure EPA, to reduce

09:59:07 23 triglyceride levels, right?

09:59:09 24 A A skilled artisan would have been what?

09:59:13 25 Q Would have found it obvious to use either pure EPA or

09:59:18 1 pure DHA to reduce triglyceride levels.

09:59:20 2 A It had been done. Yes.

09:59:22 3 Q Right. And so it would have been obvious to a skilled

09:59:27 4 artisan, as of March 2008, that purified EPA reduces

09:59:31 5 triglyceride levels, right?

09:59:32 6 A Yes, that was obvious.

09:59:36 7 Q Now, there's nothing in the EpaDEL label that warns about

09:59:42 8 LDL-C increases, correct?

09:59:45 9 A No. It's far too nebulous to warn about anything.

09:59:49 10 Q Now, multiple studies in the prior art show that EPA

09:59:53 11 reduces triglycerides, correct?

09:59:55 12 A Yes.

09:59:57 13 MR. KLEIN: Let's go DDX 10.13.

09:59:57 14 BY MR. KLEIN:

10:00:03 15 Q All right. And this is DX 1538, which is the Mori

10:00:07 16 reference you discussed on direct, right?

10:00:09 17 A Yes.

10:00:09 18 Q And the title of Mori is "Purified EPA and DHA Have"

10:00:19 19 Differential Effects on Serum Lipids and Lipoproteins, LDL

10:00:25 20 Particle Size, Glucose, and Insulin in Mildly Hyperlipidemic

10:00:32 21 Men," right?

10:00:32 22 A Yes.

10:00:32 23 Q And so Mori was addressing all those things.

10:00:35 24 A Yes.

10:00:35 25 Q I know you talked about some of the portions of the

10:00:38 1 article, but I want to walk through it with you.

10:00:40 2 MR. KLEIN: Let's go to DDX 10.14.

10:00:40 3 BY MR. KLEIN:

10:00:45 4 Q The background says,

10:00:49 5 "Regular consumption of n-3 fatty acids of

10:00:54 6 MARINE origin can improve serum lipids and reduce

10:00:58 7 cardiovascular risk."

10:00:59 8 That was known at the time Mori published the

10:01:05 9 2000 reference, right?

10:01:06 10 A Well, we -- no. Regular consumption of omega-3 fatty

10:01:12 11 acids of MARINE origin can improve serum lipids, yes. But

10:01:16 12 reduce cardiovascular risk? No. There was no foundation for

10:01:20 13 that.

10:01:20 14 MR. KLEIN: All right. Let's go to the next

10:01:21 15 portion, the objective -- I'm sorry, it's 10.15.

10:01:21 16 BY MR. KLEIN:

10:01:28 17 Q The objective of the Mori study was to determine whether

10:01:33 18 EPA and DHA acids have differential effects on serum lipids.

10:01:38 19 That was one the objectives, right?

10:01:41 20 A Yes.

10:01:41 21 MR. KLEIN: Okay. And let's go to DDX 10.16,

10:01:46 22 and, for the record, we're still on 1538, page 1.

10:01:46 23 BY MR. KLEIN:

10:01:51 24 Q Now, the design was a double-blind, placebo-controlled

10:01:57 25 trial that used 4 grams purified EPA, 4 grams purified DHA,

10:02:01 1 and a placebo, which was olive oil, right?

10:02:05 2 A Yes.

10:02:06 3 MR. KLEIN: Okay. Let's go to DDX 10.17.

10:02:06 4 BY MR. KLEIN:

10:02:14 5 Q And the purity of EPA used in Mori was 96 percent, right?

10:02:22 6 A Yes.

10:02:22 7 Q And that's what's covered by the claims?

10:02:24 8 A Yes.

10:02:25 9 MR. KLEIN: All right. And let's go to DDX

10:02:28 10 10.18.

10:02:28 11 BY MR. KLEIN:

10:02:34 12 Q So one of the purposes of Mori 2000 was to assess whether

10:02:38 13 EPA and DHA had different effects on triglycerides, right?

10:02:42 14 A Yes.

10:02:42 15 Q Now, the article -- I can't remember if this came up in
10:02:46 16 direct, but the article uses the term "triacylglycerols."

10:02:51 17 A Triacylglycerols. Yes.

10:02:54 18 Q That's a synonym for triglycerides, right?

10:02:56 19 A One in the same.

10:02:58 20 Q Okay. And Mori concluded that triglycerides fell by
10:03:02 21 about 20 percent in the DHA group, and about 18 percent in the
10:03:08 22 EPA group, right?

10:03:09 23 A Yes.

10:03:09 24 Q Okay. And about 18 percent is pretty close to
10:03:15 25 20 percent, right?

10:03:15 1 A Yes.

10:03:16 2 Q Okay. And so it would have been obvious to a skilled
10:03:20 3 artisan, in March 2008, that 4 grams pure EPA could reduce
10:03:25 4 triglycerides by about 20 percent, right?

10:03:27 5 A Yeah. 18 percent here. Uh-huh.

10:03:30 6 MR. KLEIN: Okay. Let's go to slide DDX 10.19.

10:03:30 7 BY MR. KLEIN:

10:03:34 8 Q And then in the "Results" section, Mori says, "LDL
10:03:38 9 cholesterol...were not affected significantly by EPA," and
10:03:42 10 then "DHA increased LDL cholesterol by 8 percent," correct?

10:03:47 11 A Yes.

10:03:48 12 MR. KLEIN: Okay. The -- let's go to DDX 10.20.

10:03:48 13 BY MR. KLEIN:

10:03:57 14 Q So this has the "Results" section, and then the
10:04:00 15 "Conclusion" followed, right, in the abstract?

10:04:02 16 A Yes.

10:04:02 17 Q And the conclusion was EPA and DHA had differential
10:04:07 18 effects on lipids, right?

10:04:09 19 A Yes.

10:04:09 20 Q And so Mori isn't saying these differential effects
10:04:14 21 between EPA and DHA are due to baseline triglyceride
10:04:18 22 differences or sample size, correct?

10:04:20 23 A Well, a POSA would have looked at that and would have
10:04:25 24 drawn a conclusion on that, yes.

10:04:26 25 Q Okay. But that would -- but Mori did not say that,

10:04:29 1 **correct?**

10:04:30 2 A **No, he did not.**

10:04:31 3 Q **Okay. Mori teaches that a skill -- teaches a skilled**

10:04:34 4 **artisan that EPA and DHA have differential effects on LDL-C;**

10:04:39 5 **namely, DHA increased LDL-C by 8 percent, and it was**

10:04:44 6 **statistically significant, and EPA had no significant effect,**

10:04:49 7 **correct?**

10:04:49 8 A **Mori doesn't teach that, he states that. But, certainly,**

10:04:54 9 **Rambjør disagrees with that, and multiple other papers**

10:04:57 10 **disagreed with that.**

10:04:58 11 Q **Okay. And we'll talk about Rambjør and the other papers**

10:05:01 12 **later.**

10:05:01 13 **Now -- and you talked about other portions of Mori**

10:05:05 14 **that found other differences between EPA and DHA, correct?**

10:05:11 15 A **Yes, sir.**

10:05:12 16 Q **Okay. And you said that those other differences could**

10:05:15 17 **favor DHA?**

10:05:16 18 A **Yes, we did.**

10:05:17 19 Q **Okay. But, Mori is certainly teaching that EPA and DHA**

10:05:23 20 **have different effects on the body, right?**

10:05:25 21 A **Have different effects on --**

10:05:27 22 Q **The body.**

10:05:28 23 A **The body?**

10:05:29 24 Q **Yes.**

10:05:30 25 A **Where does he make reference to different effects on the**

10:05:33 1 **body?**

10:05:33 2 Q Well, Mori is talking about different effects in LDL-C,
10:05:37 3 different effects in particle size, different effect -- Mori
10:05:41 4 is saying EPA and DHA have different effects, right?

10:05:44 5 A Yes, he is.

10:05:45 6 Q Okay. And a skilled artisan would understand from Mori
10:05:48 7 that DHA and EPA can work differently.

10:05:51 8 A Yeah, they clearly had some different effects. Yes.

10:05:55 9 MR. KLEIN: Okay. Let's go to DDX 10.21.

10:05:55 10 BY MR. KLEIN:

10:05:58 11 Q And I -- we've seen this before, but Mori also says
10:06:02 12 elsewhere in the paper, on DDX 1538, page 3, that, "Serum LDL
10:06:09 13 cholesterol increased significantly with DHA, but not with
10:06:12 14 EPA," right?

10:06:13 15 A Yes.

10:06:13 16 Q Okay. And so the authors of Mori concluded that there
10:06:20 17 was not a statistically significant increase in LDL-C
10:06:25 18 attributed to those patients who were taking purified EPA,
10:06:30 19 correct?

10:06:30 20 A He does state that.

10:06:31 21 Q Okay. And as of March 2008, a skilled artisan could
10:06:34 22 reasonably rely on Mori 2000 as teaching that DHA, but not
10:06:39 23 EPA, increases LDL-C?

10:06:41 24 A But they would both look at a numerical increase.

10:06:48 25 Q Okay. A skilled artisan, in March 2008, could reasonably

10:06:53 1 look at the LDL-C statements in Mori 2000, and believe that a
10:06:58 2 future study assessing differential results on LDL-C, between
10:07:03 3 purified EPA and DHA, would be warranted.

10:07:07 4 Do you agree with that?

10:07:08 5 A You would want to confirm the results of a small study
10:07:12 6 like this. Yes.

10:07:14 7 Q Okay. And skilled artisan, in March 2008, would have
10:07:15 8 read Mori 2000 as teaching that 96 percent pure EPA was LDL
10:07:22 9 neutral, correct?

10:07:23 10 A Yeah. I'm not going to agree with that because of the
10:07:26 11 caveats we've already discussed, but it -- it still increased.

10:07:31 12 Q Okay. Now, Amarin, itself, read Mori, and other prior
10:07:36 13 art, as teaching that pure EPA was LDL neutral. Are you aware
10:07:40 14 of that?

10:07:41 15 A No. But, I don't speak for Amarin.

10:07:43 16 MR. KLEIN: Okay. Well, let's take a look at
10:07:46 17 DDX 10.22. And this is DX 1829, page 11, and DX 2241. And
10:07:54 18 the reason there are two documents is -- well, let me ask.

10:07:54 19 BY MR. KLEIN:

10:07:58 20 Q Were you here -- you weren't here for Dr. Ketchum's
10:08:01 21 testimony, right?

10:08:01 22 A No.

10:08:02 23 Q Have you read his testimony?

10:08:03 24 A I have not.

10:08:04 25 Q Okay. Well, the reason there are two documents is solely

10:08:07 1 to establish the date. The second document is metadata. So
10:08:11 2 I'll represent to you that the date of this Amarin document is
10:08:16 3 March 20, 2008. And you understand that that date is before
10:08:20 4 the alleged conception date of March 25th, 2008?

10:08:24 5 A Yes.

10:08:24 6 Q Okay. And Appendix 4 in this Amarin document is titled,
10:08:31 7 "EPA versus DHA Mori, et al." And you see that Amarin
10:08:39 8 describes the LDL effect of Mori as teaching that serum LDL
10:08:45 9 increases significantly with DHA, but not EPA -- what we read
10:08:49 10 in the article, right?

10:08:50 11 A Yes.

10:08:50 12 Q And at the bottom,
10:08:52 13 "Amarin concludes that Mori 2000 taught both
10:08:55 14 EPA and DHA reduced triglycerides."

10:08:58 15 Do you see that?

10:08:59 16 A Yes.

10:08:59 17 Q And then concluded,
10:09:00 18 "DHA was also associated with an increase in
10:09:04 19 LDL cholesterol," right?

10:09:06 20 A Yes.

10:09:06 21 Q Now, Amarin, in this March 20, 2008 document accurately
10:09:11 22 described the Mori reference, correct?

10:09:13 23 A They're quoting it.

10:09:15 24 MR. KLEIN: Yeah.

10:09:15 25 Okay. Let's go to DDX 10.23. This is another

10:09:21 1 Amarin document. It's DX 1862, page 47.

10:09:21 2 BY MR. KLEIN:

10:09:26 3 Q And I'll represent to you that this is a partnering
10:09:29 4 presentation, you can see it, with a company called Arisaph,
10:09:34 5 dated August 3rd, 2009.

10:09:36 6 Have you seen this document?

10:09:37 7 A I have not.

10:09:40 8 Q Okay. Well, on this slide, page 47 of the exhibit,
10:09:45 9 there's a slide that's titled "EPA, No LDL Effect."

10:09:49 10 Do you see that?

10:09:51 11 A Yes.

10:09:52 12 Q Okay. And by the date of this reference, August 2009,
10:09:56 13 there were no MARINE study results yet, right?

10:10:00 14 A Correct.

10:10:00 15 Q And below the title is a description of the Mori
10:10:06 16 reference, right?

10:10:08 17 A Yes.

10:10:09 18 Q Okay. And so Amarin told its potential partner, Arisaph,
10:10:16 19 that Mori 2000 teaches that 96 percent pure EPA, 4 grams per
10:10:23 20 day, has zero percent change in LDL, right?

10:10:27 21 A That's what it says.

10:10:28 22 Q Okay. And Amarin did not misrepresent Mori to its
10:10:32 23 potential partner Arisaph, correct?

10:10:36 24 A I can't -- apparently not.

10:10:39 25 Q Okay.

10:10:40 1 A They -- it's not something they would want to do, no.

10:10:43 2 MR. KLEIN: Let's go to DDX 10.24.

10:10:43 3 BY MR. KLEIN:

10:10:46 4 Q This is another document, DX 1800, page 10. It's another
10:10:52 5 one of these Amarin slide decks. And if you can read the
10:10:57 6 date, it says March 2010. And by March 2010, Amarin still had
10:11:05 7 no MARINE data, correct?

10:11:07 8 A Yes.

10:11:07 9 Q Okay. And I'll represent to you that Dr. Ketchum
10:11:12 10 testified that this presentation was directed to and investor
10:11:15 11 audience. Okay?

10:11:16 12 For the record, that's transcript 210, line 20, to
10:11:21 13 211, line 4. Just to orient you, Dr. Toth.

10:11:24 14 Okay. Now, here, Amarin, you can see Amarin is
10:11:28 15 distinguishing Lovaza from AMR 101.

10:11:32 16 Do you see that?

10:11:32 17 A Yes.

10:11:32 18 Q And you understand AMR 101 is the code name for Vascepa?

10:11:36 19 A Yes.

10:11:36 20 Q And under the Lovaza section for LDL effect, it says,
10:11:42 21 "elevates LDL-C."

10:11:46 22 Do you see that?

10:11:47 23 A Yes.

10:11:47 24 Q That's, obviously, not disputed, right?

10:11:49 25 A Yeah.

10:11:50 1 Q And then under the Vascepa section, you see -- I guess
10:11:54 2 there are two potential indications, but one is above
10:11:57 3 500 milligrams per deciliter, right?

10:11:59 4 A Yes.

10:11:59 5 Q And Amarin tells its investors that there's no DHA
10:12:04 6 induced elevation.

10:12:06 7 Do you see that?

10:12:07 8 A Yes.

10:12:07 9 Q Okay. And that statement to investors is consistent with
10:12:11 10 what the prior art taught, correct?

10:12:17 11 A That's a statement. But, on balance, the prior art noted
10:12:23 12 that both EPA and DHA could induce elevations in LDL.

10:12:28 13 Q Okay. So is it your testimony that when Amarin made this
10:12:31 14 presentation to investors, it was mischaracterizing the prior
10:12:35 15 art?

10:12:35 16 A No. I would never say that.

10:12:37 17 MR. KLEIN: Okay. And for the record, this is
10:12:38 18 DX 1800, page 10, in case I missed that.

10:12:41 19 Let's go DDX 10.25.

10:12:41 20 BY MR. KLEIN:

10:12:47 21 Q Here is another slide in the presentation where Amarin
10:12:50 22 tells investors "multiple studies demonstrate that DHA raises
10:12:54 23 LDL-C."

10:12:56 24 Do you see that?

10:12:56 25 A I do.

10:12:57 1 Q And you can tell that the support is all coming from the
10:13:02 2 prior art, correct?
10:13:05 3 A Yes. The references are all before 2008.
10:13:08 4 Q Okay. And let's go to the next slide, which is
10:13:11 5 DDX 10.26, and this slide says "multiple studies demonstrate
10:13:16 6 that EPA is LDL neutral."
10:13:19 7 Do you see that?
10:13:19 8 A Yes.
10:13:19 9 Q And this is Amarin's support for the representation to
10:13:24 10 investors that the prior art demonstrated EPA is LDL neutral,
10:13:31 11 right?
10:13:32 12 A It's data they're showing.
10:13:36 13 Q Right.
10:13:37 14 In fact, in the six references cited, on -- by the
10:13:41 15 way, this is page 13. I may not have said that for the
10:13:44 16 record. And the last one was page 12 -- but on this slide,
10:13:49 17 page 13, Amarin cited six references, all dated before 2008,
10:13:53 18 correct?
10:13:53 19 A Yes.
10:13:54 20 Q And those references include the Mori 2000 reference,
10:13:57 21 correct?
10:14:00 22 A Not on this page.
10:14:01 23 Q It's highlighted.
10:14:03 24 A Mori --
10:14:06 25 Q On the left.

10:14:07 1 A Oh, okay. Yes. Okay.

10:14:08 2 Q Okay. And you can see that what Amarin is telling its

10:14:12 3 investors in 2010, is that Mori reported a zero percent change

10:14:17 4 in LDL, right?

10:14:19 5 A Zero point zero zero.

10:14:22 6 Q And Amarin is also citing Kurabayashi, right?

10:14:25 7 A Yes.

10:14:25 8 Q And that's one of the references that you understand the

10:14:27 9 defendants' are relying on, right?

10:14:29 10 A Yes.

10:14:29 11 Q And for Kurabayashi, Amarin is telling investors that LDL

10:14:35 12 will reduce by 6 percent, right?

10:14:38 13 A Yes.

10:14:39 14 Q Okay. And you're not testifying that Amarin

10:14:42 15 mischaracterized the Mori and the Kurabayashi references to

10:14:46 16 its investors, correct?

10:14:48 17 A I am not.

10:14:49 18 MR. KLEIN: Okay. Let's go to DDX 10.27, and

10:14:58 19 this is DX 1741, pages 1, 7, and 9.

10:14:58 20 BY MR. KLEIN:

10:15:02 21 Q And do you recognize this as the Bays article from 2011?

10:15:08 22 A I do.

10:15:09 23 And, counsel, I need to pull this article up.

10:15:12 24 What's the --

10:15:13 25 Q It's DX 1741.

10:15:14 1 A Yes.

10:15:15 2 Q Hopefully, it's in the binder.

10:15:25 3 A Excuse me just one second. It's an awful lot of papers.

10:15:46 4 1741.

10:15:46 5 Okay. I have it, counsel.

10:15:48 6 Q Okay. Let me know when you're ready.

10:15:50 7 A Which page is this exhibit?

10:15:52 8 Q Let's focus on pages 7 and 9. And 9, I believe, is just

10:15:57 9 the footnote.

10:16:06 10 A Seven. Refresh my memory how the numbering goes here.

10:16:15 11 You're using the journal page number, right?

10:16:17 12 Q No. I'm using the -- there should be a DX 1741 on the

10:16:21 13 bottom?

10:16:21 14 A Okay.

10:16:22 15 Q And then it's page 9 of that exhibit cite.

10:16:24 16 A Okay. Page 9 is the references.

10:16:28 17 Q Yeah. I'm sorry. Page 7 -- you probably want to look at

10:16:32 18 page 7 because page 9 is just the footnote.

10:16:34 19 A Okay. Can you please direct me to where on the page it

10:16:39 20 is -- I have it.

10:16:40 21 Q Okay. You got it?

10:16:41 22 A Yes.

10:16:41 23 Q Okay. Now, just for some context, you understand this

10:16:45 24 article reported on the MARINE study results in 2011, right?

10:16:49 25 A Yes.

10:16:50 1 Q And you know Dr. Bays, correct?

10:16:52 2 A I do.

10:16:52 3 Q And do you have a lot of respect for Dr. Bays?

10:16:56 4 A Sure. Of course.

10:16:57 5 Q And Dr. Bays wrote, in DX 1741, that,

10:17:01 6 "In several small studies, although DHA

10:17:05 7 treatment generally increased LDL cholesterol levels,

10:17:09 8 EPA therapy did not."

10:17:11 9 Do you see that?

10:17:12 10 A I do.

10:17:12 11 Q And in support, among other cites, Dr. Bays cited the

10:17:22 12 Mori article from 2000, right?

10:17:24 13 A Yes.

10:17:24 14 Q And Dr. Bays did not mischaracterize the Mori article,

10:17:28 15 right?

10:17:28 16 A No. He wouldn't do that.

10:17:30 17 I'm just reading, counsel. Give me 30 seconds.

10:17:43 18 Okay. Go ahead.

10:17:47 19 Q You got it?

10:17:47 20 A I do.

10:17:48 21 Q Okay.

10:17:49 22 A But, he also notes that,

10:17:50 23 "These previous studies were generally in

10:17:53 24 patients with normal to borderline triglycerides and

10:17:55 25 none included patients with very high triglycerides."

10:17:58 1 Q Right. And we know that from Mori. I didn't say Mori
10:18:02 2 treated very high triglyceride patients.

10:18:04 3 A Okay.

10:18:04 4 MR. KLEIN: Okay. Let's go to DDX 10.28.

10:18:04 5 BY MR. KLEIN:

10:18:11 6 Q One of the other references -- we're now on page 9, DDX

10:18:24 7 1741. Dr. Bays also says,

10:18:27 8 "Smaller trials suggested that purified EPA

10:18:30 9 might reduce triglyceride levels without increasing

10:18:33 10 the LDL cholesterol levels."

10:18:35 11 Do you see that?

10:18:37 12 A I do. But, again, page 9 is the references.

10:18:41 13 Q Maybe the note -- I might have a wrong page number.

10:18:50 14 MS. HUTTNER: It's page 1.

10:18:51 15 MR. KLEIN: It's page 9?

10:18:53 16 MS. HUTTNER: No. It's 1.

10:18:54 17 MR. KLEIN: Oh. It's page 1.

10:18:54 18 THE WITNESS: Page 1.

10:18:56 19 MR. KLEIN: Yes. It's right above Methods --
20 oh, I see. It does say 1. Okay.

21 THE WITNESS: It's just above Methods, on page
22 1?

23 MR. KLEIN: It looks like three sentences above
24 Methods, on the column on the right-hand side.

25 THE WITNESS: Yes, I have it. "Smaller trials

1 of patients with normal to moderate" -- Okay.

2 Thank you.

3 **BY MR. KLEIN:**

10:19:33 4 Q All right. I'll start again so the record is clear.

10:19:35 5 On page 1, Dr. Bays says,

10:19:39 6 "Smaller trials of patients with normal to

10:19:43 7 moderately elevated triglyceride levels suggested

10:19:45 8 that purified EPA might reduce triglyceride levels

10:19:48 9 without increasing the LDL cholesterol levels."

10:19:51 10 That's what Dr. Bays said in the article, right?

10:19:54 11 A Yes.

10:19:54 12 Q And he cited, among other references, the Kurabayashi

10:19:57 13 reference, right?

10:19:59 14 A Yes.

10:19:59 15 Q And Dr. Bays did not mischaracterize the Kurabayashi

10:20:06 16 reference, correct?

10:20:07 17 A That's his interpretation. I would never suggest he

10:20:10 18 mischaracterized. But, papers are subject to interpretation.

10:20:15 19 MR. KLEIN: Now, let's move on to DDX 10.30.

10:20:15 20 **BY MR. KLEIN:**

10:20:29 21 Q This is the Rambjør article, DX 1961. And I've got

10:20:35 22 page 3 on the screen.

10:20:36 23 You talked about this one on direct, right?

10:20:38 24 A Yes.

10:20:38 25 Q And Rambjør summarizes the results of three small

10:20:44 1 **separate studies, right?**

10:20:46 2 A **Yes.**

10:20:47 3 Q **And there were nine patients who took DHA, right?**

10:20:52 4 A **Yes.**

10:20:52 5 Q **And 25 took EPA?**

10:20:54 6 A **Yes.**

10:20:55 7 Q **And the dose was 3 grams per day, right?**

10:20:58 8 A **Um --**

10:21:01 9 Q **It's in the middle.**

10:21:02 10 A **It's -- EPA -- yes.**

10:21:06 11 Q **Okay. And Mori used 4 grams, right?**

10:21:11 12 A **Yes.**

10:21:11 13 Q **And the claims require 4 grams, right?**

10:21:14 14 A **Yes.**

10:21:15 15 MR. KLEIN: **Okay. Let's go to DDX 10.31.**

10:21:15 16 **BY MR. KLEIN:**

10:21:20 17 Q **And in the abstract, Rambjør studied 91 percent pure EPA,**

10:21:26 18 **right?**

10:21:26 19 A **Yes.**

10:21:26 20 Q **Okay. And you said omega-3s are complex, right? So that**

10:21:32 21 **other 9 percent, we have no idea what that is, right?**

10:21:34 22 A **That's right.**

10:21:35 23 Q **Okay. Mori used 96 percent pure EPA, correct?**

10:21:39 24 A **Yes.**

10:21:40 25 Q **And the claims require 96 percent pure EPA, right?**

10:21:44 1 A Yes.

10:21:45 2 MR. KLEIN: Let's go to DDX 10.32.

10:21:45 3 BY MR. KLEIN:

10:21:50 4 Q And here, Mori says that,

10:21:53 5 "The percent change in LDL-C was identical

10:21:58 6 for both EPA and DHA, plus 6 percent; but the smaller

10:22:02 7 number of subjects in the latter group prevented the

10:22:05 8 difference from being significant," right?

10:22:07 9 A Yeah. Sort of a similar conclusion to Mori, yeah.

10:22:10 10 Q Right. Well -- and then Rambjør says,

10:22:14 11 "Further studies are needed to clearly define

10:22:18 12 individual effects of EPA and DHA on human lipid

10:22:23 13 metabolism," right?

10:22:23 14 A Yes.

10:22:23 15 Q Okay. And Mori 2000 is actually one of those further

10:22:27 16 studies that did that, correct?

10:22:28 17 A Yes.

10:22:29 18 MR. KLEIN: Okay. Let's go to DDX 10.33.

10:22:29 19 BY MR. KLEIN:

10:22:32 20 Q And Mori referenced the Rambjør paper, right?

10:22:39 21 A Yeah -- um, Mori -- may I see it?

10:22:43 22 Q Well, it's on the screen.

10:22:45 23 A Okay.

10:22:45 24 Q You can look at it, too. It's DDX 1538.

10:22:49 25 A 1538.

10:22:50 1 Q **Page 1.**

10:22:58 2 A **Counsel, you said page 1?**

10:23:01 3 Q **Yes.**

10:23:06 4 A **I have it.**

10:23:07 5 Q **Yeah. It's near the bottom of the second column.**

10:23:13 6 A **I have it.**

10:23:14 7 Q **Okay. And Mori said that,**

10:04:54 8 "Rambjør concluded that EPA is responsible

10:23:20 9 for the triglyceride lowering effect of fish oils in

10:23:26 10 humans, but their study had small numbers of subjects

10:23:30 11 and was of short duration," correct?

10:23:31 12 A **Yeah, but they actually had 25 patients in the EPA arm**

10:23:35 13 **and Mori had 19.**

10:23:37 14 Q **Okay. But Mori concluded that its study was superior to**

10:23:42 15 **the one in Rambjør because it's criticizing Rambjør, correct?**

10:23:45 16 A **Well, they had more patients in Rambjør.**

10:23:48 17 Q **Okay. But can we agree that Mori is critiquing the study**

10:23:51 18 **in Rambjør?**

10:23:52 19 A **Critiquing it? Where is he critiquing?**

10:23:57 20 Q **But that their study had small numbers of subjects and**

10:24:01 21 **was of short duration?**

10:24:02 22 A **Yeah. I don't know how he can critique it when the EPA**

10:24:07 23 **group had 25 and they had 19.**

10:24:08 24 **That's incongruous to me. The DHA group was**

10:24:11 25 **smaller, but 25 in Rambjør, 19 in Mori, I don't see how Mori**

10:24:18 1 could criticize that study being smaller.

10:24:21 2 Q Okay. But a skilled artisan looking at Mori will see

10:24:24 3 Mori's comments with regard to the earlier Rambjør study,

10:24:29 4 correct?

10:24:29 5 A Sure. They can read it.

10:24:31 6 MR. KLEIN: Yeah.

10:24:31 7 Let's go to DDX10.34.

10:24:31 8 BY MR. KLEIN:

10:24:34 9 Q This is DX 1605, the von Schacky paper from 2006. And

10:24:40 10 I'm on page 9.

10:24:41 11 A Yes.

10:24:41 12 Q You talked about this one on direct, right?

10:24:43 13 A Yes.

10:24:43 14 Q And I think you agree that it's a review article, right?

10:24:47 15 A Yes.

10:24:47 16 Q So von Schacky is not presenting any new data.

10:24:51 17 A No. It would be a synthesis of the available data.

10:24:55 18 Q Okay. And you relied on this Table 1 from von Schacky,

10:24:59 19 right?

10:24:59 20 A Yes.

10:24:59 21 Q And this chart talks about semi-quantitatively reflecting

10:25:05 22 the findings from the literature?

10:25:06 23 A Yes.

10:25:07 24 Q This chart, though, is not very scientific.

10:25:10 25 Do you agree?

10:25:11 1 A Oh, I disagree.

10:25:12 2 Q You think this is a -- you can tell whether there

10:25:14 3 was statistically significant results for LDL-C from the

10:25:18 4 literature from this chart?

10:25:19 5 A That's not the point. It's a chart to synthesize a large

10:25:23 6 amount of data from different papers, and people find charts

10:25:27 7 like this very valuable because, at a glance, it gives you a

10:25:31 8 summary of changes, and also provides you with a feel for

10:25:34 9 magnitude of change.

10:25:35 10 Q Okay. And can you agree that this chart is on a very,

10:25:40 11 very high level?

10:25:41 12 That's the goal, right?

10:25:42 13 A A very, very, high level?

10:25:44 14 Q Well, this chart is trying to synthesize the literature

10:25:48 15 at a very high level.

10:25:49 16 Do you agree?

10:25:50 17 A Oh, sure.

10:25:51 18 Q And this is not getting into the details of what -- what

10:25:54 19 studies in the literature actually showed.

10:25:56 20 A Well, it does get at what the studies actually showed.

10:26:00 21 It just provides you with a semi-quantitative presentation of

10:26:05 22 that information.

10:26:06 23 Q Okay. And then in the notes on Table 1, von Schacky

10:26:10 24 talks about Rambjørn and Mori, among other references, right?

10:26:13 25 A Yes, he does.

10:26:15 1 Q Okay. Now, on direct, you didn't talk about any of the
10:26:18 2 text from this article, right?

10:26:19 3 A The text?

10:26:20 4 Q Yes.

10:26:21 5 A Oh. We can.

10:26:22 6 MR. KLEIN: Let's go to DDX 10.125.

10:26:26 7 THE WITNESS: Which, uh --

10:26:26 8 BY MR. KLEIN:

10:26:27 9 Q It's going to go on the screen and it's page -- it's DX
10:26:34 10 1605, page 5. And you should be able to find it because the
10:26:38 11 heading is there.

10:26:38 12 A 1605?

10:26:40 13 Q Yes.

10:26:48 14 A I have it.

10:26:49 15 Q Okay. And you see the heading is "EPA versus DHA"?

10:27:02 16 A Yes.

10:27:03 17 Q And what the author here says with regard to Mori 2000,
10:27:08 18 is that,

10:27:09 19 "In more recent comparative studies, no
10:27:12 20 effects of either EPA or DHA were seen on total --
10:27:16 21 were seen on LDL levels."

10:27:18 22 Do you see that?

10:27:20 23 A Yes.

10:27:20 24 Q And by the way, with regard to Rambjør, on the last
10:27:26 25 sentence, it says,

10:27:28 1 "After either EPA or DHA, no clear-cut
10:27:32 2 effects on HDL were demonstrated."
10:27:34 3 Do you see that?
10:27:35 4 A Yes. But, that's just for those five papers.
10:27:38 5 Q Right. And that's citing Rambjør -- it's not citing
10:04:54 6 Rambjør for the effects on LDL, correct?
10:27:44 7 A Yes. But, clearly, he included that in the table.
10:27:48 8 Q Okay. What von Schacky said about Mori, when he said "no
10:27:54 9 effects of either EPA or DHA were seen on LDL," that's
10:27:59 10 incorrect, right?
10:28:00 11 A What sentence is that?
10:28:03 12 Q The one that I have highlighted.
10:28:06 13 "In more recent comparative studies, no
10:28:08 14 effects of either EPA or DHA were seen on LDL
10:28:12 15 levels."
10:28:12 16 That's not what Mori said, right?
10:28:15 17 A Correct.
10:28:16 18 MR. KLEIN: Let's go to DDX 10.126.
10:28:16 19 BY MR. KLEIN:
10:28:22 20 Q And this is a demonstrative that compares DX 1605,
10:28:27 21 page 5, which is von Schacky, to DX 1538, page 1, which is
10:28:33 22 Mori. And Mori held that the effects of DHA were seen on LDL
10:28:40 23 levels, and they were significant, correct?
10:28:42 24 A Yes.
10:28:43 25 Q And so von Schacky did not even characterize the Mori

10:28:46 1 2000 -- did not even accurately characterize the Mori
10:28:52 2 2000 reference, correct?
10:28:53 3 A Well, it would have been his interpretation.
10:28:56 4 Q Okay. Now, clearly, a skilled artisan, as of March 2008,
10:29:00 5 looking at the literature, including the von Schacky
10:29:02 6 reference, would look at the underlying clinical studies, such
10:29:06 7 as Mori, right?
10:29:07 8 A Yes.
10:29:16 9 MR. KLEIN: All right. Let's go to DDX 10.123.
10:29:16 10 BY MR. KLEIN:
10:29:26 11 Q Okay. This is a snapshot of PX 833, which is a document
10:29:30 12 that you discussed on direct.
10:29:32 13 Do you remember that?
10:29:32 14 A I do.
10:29:33 15 Q Okay. And the document is titled "The Editor's
10:29:37 16 Roundtable Hypertriglyceridemia," right?
10:29:40 17 A Yes.
10:29:40 18 Q And you testified that this article showed praise of the
10:29:45 19 MARINE study; in particular, the LDL neutral effect, right?
10:29:48 20 A Yes.
10:29:48 21 Q Okay. Now we're at -- PX 833, page 1, discloses that the
10:29:54 22 article is sponsored by a grant from Amarin, right?
10:30:03 23 You can see that in that middle box?
10:30:03 24 A Yes.
10:30:05 25 Q And the article discloses that Drs. Ballantyne, Bays, and

10:30:10 1 Jones have all received compensation from Amarin, right?

10:30:13 2 A Yes.

10:30:13 3 Q And you didn't mention this on your direct testimony,

10:30:17 4 right?

10:30:18 5 A No.

10:30:19 6 Q Okay. Now, Dr. Toth, this isn't industry praise. It's

10:30:24 7 self-praise, correct?

10:30:26 8 A Well, no. I'm sure these -- well, I know all of these

10:30:29 9 guys, and they would be able to differentiate themselves from

10:30:34 10 whether or not it's coming from them, or because they're

10:30:36 11 somehow sponsored by industry.

10:30:38 12 Q Do you consider an article sponsored by Amarin as

10:30:41 13 objective evidence of praise by, by the -- a community?

10:30:50 14 That's a stretch, right?

10:30:51 15 A Well, what Harold said in this paper, he also said in the

10:30:58 16 paper on the MARINE Trial. So there's no -- there's no

10:31:00 17 discrepancy there.

10:31:01 18 Q Okay. But, the article was sponsored by Amarin, correct?

10:31:04 19 A Yes. It's indisputable.

10:31:07 20 Q Let's switch gears.

10:31:09 21 Again, all patent claims require 4 grams of purified

10:31:13 22 EPA, right?

10:31:13 23 A Yes.

10:31:14 24 Q And Lovaza is a 4-gram combination of EPA, DHA and

10:31:19 25 whatever else is in there.

10:31:20 1 A Correct.

10:31:21 2 Q Okay. And as of March 2008 -- well, I think you said
10:31:25 3 that.

10:31:26 4 Okay. A number -- now, on direct -- I want to
10:31:39 5 clarify something that you said yesterday. On direct, you
10:31:43 6 said that the medical literature provided a reason not to use
10:31:47 7 a 4-gram dose of and omega-3 fatty acid to treat severe
10:31:52 8 hypertriglyceridemia.

10:31:53 9 Do you remember that, in the context of whether a
10:31:55 10 4-gram dose would be obvious?

10:31:58 11 A You know, I don't remember that.

10:32:00 12 Can you say that one more time, please, counsel.

10:32:02 13 Q Yes. So -- I won't put it up -- but you were asked, on
10:32:09 14 page 167 of the rough,

10:32:15 15 "As of March 2008, did the medical literature
10:32:18 16 provide a reason not to use a 4-gram dose of and
10:32:23 17 omega-3 fatty acid?"

10:32:23 18 And you said, "Yes."

10:32:24 19 A Oh, yeah. That was citing the paper, I believe by
10:32:33 20 Nilsen. I might be wrong on the specific paper.

10:32:35 21 Q I believe that's correct.

10:32:36 22 A But, it was one that evaluated 300 patients with
10:32:40 23 myocardial infarction. And they, in the discussion,
10:32:43 24 speculated that, perhaps, they had exceeded some critical
10:32:47 25 threshold beyond which there might be toxicity instead of

10:32:51 1 benefit.

10:32:52 2 Q Okay. But as of March 2008, a skilled artisan would be
10:32:55 3 very well aware that the FDA had approved a 4-gram fish oil
10:32:59 4 product to treat severe hypertriglyceridemia, right?

10:33:02 5 A Yes.

10:33:03 6 MR. KLEIN: Okay. Now, let's go to DDX 10.35.

10:33:03 7 BY MR. KLEIN:

10:33:16 8 Q Oh, yeah. And Mori disclosed a clinical trial that used
10:33:21 9 4-gram of pure EPA, right?

10:33:23 10 A Yes.

10:33:23 11 Q And other prior art studies disclosed 4 grams of pure EPA
10:33:27 12 to reduce triglycerides as well, right?

10:33:29 13 A Yeah, there were some.

10:33:31 14 MR. KLEIN: Okay. Let's go to DDX 10.36.

10:33:31 15 BY MR. KLEIN:

10:33:34 16 Q And this is DX 2263. Do you recognize this as the
10:33:39 17 Woodman 2002 reference?

10:33:41 18 A Yes.

10:33:41 19 Q And this is prior art, correct?

10:33:45 20 MR. KLEIN: And, Your Honor, I move into
10:33:47 21 evidence DX 2263.

10:33:51 22 THE COURT: Any objection?

10:33:53 23 MR. ELIKAN: None.

10:33:53 24 THE COURT: 2263 is admitted.

10:33:53 25 (Defendants' Exhibit 2263 received in
10:33:57 evidence.)

10:33:57 1 BY MR. KLEIN:

10:33:57 2 Q Okay. And Woodman 2002 disclosed a clinical trial in
10:34:01 3 which 4 grams per day of purified EPA was administered to
10:34:03 4 reduce triglycerides, correct?

10:34:03 5 A Yes.

10:34:04 6 MR. KLEIN: Let's go DDX 10.37.

10:34:04 7 BY MR. KLEIN:

10:34:10 8 Q Woodman also found that 4 grams per day reduced -- 4
10:34:16 9 grams per day of purified EPA decreased triglycerides by 19
10:34:22 10 percent, right?

10:34:23 11 A Yes.

10:34:23 12 Q And so that's about 20 percent, correct?

10:34:25 13 A Yes.

10:34:25 14 Q And DDX 10.38, this is DX 2258, page 1. Do you recognize
10:34:32 15 this as the Woodman 2003 reference?

10:34:35 16 A Yes.

10:34:35 17 Q Okay. And this is prior art, right?

10:34:37 18 A Yes.

10:34:38 19 MR. KLEIN: I move into evidence 2258.

10:34:45 20 THE COURT: Any objection?

10:34:47 21 MR. ELIKAN: None, Your Honor.

10:34:48 22 THE COURT: 2258 is admitted.

10:34:48 23 (Defendants' Exhibit 2258 received in
10:34:51 24 evidence.)

BY MR. KLEIN:

10:34:52 25 Q Woodman 2003 discloses clinical trial in which a 4-gram

10:34:55 1 per day purified EPA dose was used to reduce triglycerides,
10:34:59 2 right?

10:35:00 3 A Yes, for six weeks.

10:35:02 4 MR. KLEIN: Okay. Let's go DDX 10.39.

10:35:02 5 BY MR. KLEIN:

10:35:05 6 Q And Woodman also found that EPA and DHA significantly
10:35:09 7 decreased serum triglycerides by a similar extent relative to
10:35:13 8 placebo, right?

10:35:13 9 A Yes.

10:35:16 10 MR. KLEIN: Let's go to DDX 10.40.

10:35:22 11 This is DX 2264 --

10:35:24 12 THE COURT: Mr. Klein, before you proceed
10:35:25 13 to 2264, would this be a good time for us to take our morning
10:35:30 14 break?

10:35:30 15 MR. KLEIN: We can do that.

10:35:31 16 THE COURT: All right. I'll note that you were
10:35:33 17 about to introduce 2264. And we'll take our morning recess.

10:35:36 18 Thank you.

(A recess was taken.)

10:53:16 19
10:53:16 20 THE COURT: Please be seated.

10:53:43 21 Mr. Klein?

10:53:44 22 MR. KLEIN: Thank you, Your Honor.

10:53:44 23 BY MR. KLEIN:

10:53:46 24 Q Welcome back, Dr. Toth.

10:53:48 25 We were on DDX 10.40, which is DX2264.

10:53:53 1 Do you recognize this as the Grimsgaard 1998
10:53:56 2 reference?

10:53:56 3 A Yes.

10:53:56 4 Q Okay. And this one is prior art, right?

10:54:00 5 A Yes.

10:54:03 6 MR. KLEIN: I'd move this into evidence,
10:54:04 7 DDX 2264.

10:54:08 8 MR. ELIKAN: No objection.

10:54:10 9 THE COURT: 2264 is admitted.

10:54:10 10 (Defendants' Exhibit 2264 received in
10:54:12 11 evidence.)

10:54:12 11 BY MR. KLEIN:

10:54:13 12 Q Grimsgaard 1998 is another reference that disclosed
10:54:17 13 4 grams of pure EPA, right?

10:54:17 14 A Yes.

10:54:17 15 MR. KLEIN: Okay. Let's go to DDX 10.41. This
10:54:23 16 is DX 1545.

10:54:23 17 BY MR. KLEIN:

10:54:26 18 Q Do you recognize this as the Park reference from 2003?

10:54:31 19 A I don't recall this, but I see the paper in front of me.

10:54:35 20 Q Okay. And this is, obviously, prior art, right?

10:54:38 21 A Yes.

10:54:39 22 MR. KLEIN: Okay. I'd move into evidence
10:54:41 23 DX 1545.

10:54:43 24 MR. ELIKAN: No objection.

25 ///

10:54:45 1 BY MR. KLEIN:

10:54:45 2 Q And Park discusses a study that used 4 grams per day of
10:54:49 3 purified EPA to reduce triglycerides, right?

10:54:52 4 A Yes.

10:54:52 5 Q Let's go to --

10:54:52 6 THE COURT: And let me interject. 1545 is
10:54:56 7 admitted.

10:54:56 8 (Defendants' Exhibit 1545 received in
10:54:58 9 evidence.)

MR. KLEIN: Oh, I'm sorry.

10:54:58 10 Okay. Let's go to DDX 10.42. This is DX 1551.

10:54:58 11 BY MR. KLEIN:

10:55:04 12 Q Do you recognize this as the Wojenski article from 1990?

10:55:09 13 A Yes.

10:55:10 14 Q And I believe this one is in evidence.

10:55:16 15 Wojenski is prior art, right?

10:55:18 16 A Yes.

10:55:18 17 Q And Wojenski disclosed a clinical trial with 4 grams per
10:55:23 18 day of pure EPA, right?

10:55:24 19 A Yes.

10:55:25 20 Q So, to recap, there are at least six prior art
10:55:28 21 references, Mori 2000, Wojenski, Woodman 2002, Grimsgaard
10:55:35 22 1998, Woodman 2003, and Park, that disclosed the use of
10:55:43 23 4 grams per day of purified EPA to reduce triglycerides,
10:55:48 24 right?

10:55:48 25 A Yes.

10:55:48 1 Q Okay. Now, are you offering the opinion, today, that as
10:55:52 2 of March 2008, using 4 grams per day of purified EPA to reduce
10:55:58 3 triglycerides would not be obvious?

10:56:02 4 A It would not be obvious in very high triglycerides. But,
10:56:08 5 these papers didn't look at very high triglycerides. So this
10:56:11 6 would be -- it was used in patients with triglycerides less
10:56:15 7 than 500.

10:56:15 8 Q Okay. So it certainly would be obvious to use 4 grams
10:56:19 9 pure EPA to reduce triglycerides in patients below 500, right?

10:56:23 10 A Yes. It was done.

10:56:24 11 Q And in order for it to be obvious above 500, are you
10:56:34 12 saying there would need to be a clinical study addressing 4
10:56:38 13 grams pure EPA, reducing triglycerides in patients above 500?

10:56:43 14 A Well, yes, we would like to see that.

10:56:45 15 Q Okay. Now, you don't know if that's the appropriate
10:56:48 16 legal standard, correct?

10:56:50 17 A I'm not sure.

10:56:57 18 Q Now, as of March 2008, can we agree that the prior art
10:57:01 19 would have at least motivated a skilled artisan to use 4 grams
10:57:06 20 per day of pure EPA in patients above 500?

10:57:09 21 A No, I would not agree to that.

10:57:13 22 Q Okay. So your opinion is the prior art wouldn't have
10:57:17 23 even motivated a skilled artisan to use 4 grams per day of per
10:57:22 24 EPA in a patient population that has triglycerides above 500?

10:57:27 25 A That's correct.

10:57:29 1 Q Now, there were a finite number of pure EPA doses that
10:57:34 2 were generally used in the prior art, do you agree?

10:57:37 3 A Yes.

10:57:37 4 Q Okay. And generally, they were within the range of
10:57:40 5 2 grams to 4 grams a day, right?

10:57:43 6 A They were all over the place.

10:57:44 7 Q But most of them, the focus of the successful trials was
10:57:49 8 on 2 grams to 4 grams; is that right?

10:57:51 9 A I would have to look. I would have to look at what each
10:57:54 10 one showed. But it's probably not unreasonable. But, I'm
10:57:59 11 sure there were papers with lower doses as well.

10:58:02 12 MR. KLEIN: Okay. Let's look at a document for
10:58:03 13 reference, DDX 10.44. This is DX 1862, page 93.

10:58:14 14 This is going back to that Amarin presentation
10:58:17 15 from August 3, 2009, and I'm using this as a reference because
10:58:23 16 here Amarin went through a bunch of prior art clinical
10:58:27 17 studies, and you can see -- actually, let's go back to DDX
10:58:31 18 10.43 because that might be a little easier to read.

10:58:31 19 BY MR. KLEIN:

10:58:35 20 Q Okay. So can you see that what Amarin did back in 2009
10:58:39 21 was just summarize the doses used in various prior art
10:58:43 22 references. Do you see that?

10:58:45 23 A I do.

10:58:45 24 Q And generally, most of them are in the 2 to 4 range.
10:58:48 25 Do you see that?

10:58:49 1 A Yeah, to me, most of them are in the 1.8 to 2.7 range.

10:58:53 2 MR. KLEIN: Okay. Now, let's go back to 10.44.

10:58:53 3 BY MR. KLEIN:

10:58:57 4 Q And it's the same document, but underneath you see,

10:59:01 5 "Amarin concluded that the analysis provides

10:59:04 6 reasonable evidence that doses of 2 to 4 grams per

10:59:07 7 day will be at or close to the maximum triglyceride

10:59:10 8 lowering activity of EPA."

10:59:12 9 Do you see that?

10:59:13 10 A I do see that.

10:59:13 11 Q That's a reasonable reading of the prior art with regard

10:59:17 12 to dosing, correct?

10:59:18 13 A Yeah. I'd have to say based on the studies shown here,

10:59:22 14 yes.

10:59:22 15 Q And that's a finite number of available doses for pure

10:59:29 16 EPA, correct?

10:59:30 17 A Well, yeah, it's finite, but these, by no means,

10:59:34 18 established optimal. But, they are two doses you could have

10:59:38 19 used. Yes.

10:59:39 20 Q Okay. Now, given that purified EPA lowered triglyceride

10:59:47 21 levels in patients below 500, you'd want to see if it also

10:59:51 22 lowered triglyceride levels in patients above 500, correct?

10:59:55 23 A Sure. You could try them, among the myriad of other

10:59:58 24 possibilities. But, yes, it would be of clinical interest.

11:00:01 25 Q Yeah. And it would have been of clinical interest back

11:00:04 1 in March 2008, right?

11:00:06 2 A Sure.

11:00:06 3 Q And now the reason for distinguishing between patients

11:00:10 4 below 500 and above 500 relates to pancreatitis risk, right?

11:00:15 5 A Yes. But, also reducing cardiovascular risk.

11:00:19 6 Q Right. But that 500 level is -- you talked about it in

11:00:24 7 ATP III -- that's really set because above 500, doctors should

11:00:29 8 be primarily concerned about pancreatitis risk, right?

11:00:31 9 A Well, that was the first priority. The second priority

11:00:35 10 was reducing cardiovascular risk.

11:00:38 11 Q Right. But that's why the 500 threshold is set for that

11:00:41 12 first priority, correct?

11:00:43 13 A Yes.

11:00:43 14 Q Okay. Now -- and you talked about how pancreatitis is a

11:00:45 15 serious condition, right?

11:00:46 16 A Yes. I sure did.

11:00:48 17 Q And so that 500-milligram threshold is set conservatively

11:00:52 18 to make sure you capture patients before they get

11:00:55 19 pancreatitis, right?

11:00:56 20 A You want to capture and identify as many people at risk
11:01:00 21 as possible.

11:01:00 22 Q Okay. And that 500 threshold has nothing to do with how

11:01:05 23 a drug is going to affect LDL, right?

11:01:08 24 A The 500 threshold does, in fact, identify another
11:01:13 25 group of patients who responds very differently to

11:01:16 1 triglyceride-lowering medications in terms of how their
11:01:21 2 LDL increases. It very much defines a separate population.
11:01:25 3 Q All right. And listen carefully to the question, please.
11:01:28 4 The 500 threshold was not set because above 500 you
11:01:32 5 are expected to have a greater increase in LDL-C in response
11:01:35 6 to a drug like Vascepa, correct?
11:01:38 7 A That's correct. But, people were aware of the problem.
11:01:42 8 Q Okay. And a skilled artisan would know that a drug that
11:01:46 9 reduces triglycerides in a patient at 400, is very likely to
11:01:51 10 also reduce triglycerides in a patient at 600, right?
11:01:54 11 A Yeah. I don't think that would be contested.
11:01:56 12 Q Okay. And so based on the prior art, a skilled artisan,
11:02:01 13 as of March 2008, would have reasonably expected purified EPA
11:02:06 14 to reduce triglyceride levels above 500, right?
11:02:09 15 A Yeah.
11:02:14 16 MR. KLEIN: Let's go to DDX 10 point -- hold on.
11:02:24 17 Okay. Let's go to DDX 10.45, and this is DX
11:02:37 18 1705, page 6.
11:02:37 19 BY MR. KLEIN:
11:02:38 20 Q This is a sentence from your response of expert report,
11:02:42 21 and I want to clarify whether this is an opinion you're
11:02:45 22 presenting today.
11:02:46 23 So, in your expert report, you said,
11:02:48 24 "A person of ordinary skill, in March 2008,
11:02:51 25 would not have been motivated to use a composition of

11:02:55 1 high purity EPA and substantially no DHA to lower
11:03:00 2 triglycerides in persons with very high
11:03:03 3 triglycerides."

11:03:03 4 Are you offering that opinion today and
11:03:06 5 yesterday?

11:03:06 6 A I sure am.

11:03:07 7 Q Okay. Now, that's a pretty extreme position in view of
11:03:13 8 the prior art, wouldn't you say?

11:03:14 9 A Oh, not at all.

11:03:16 10 Q Okay. Doctor, using purified EPA to treat patients with
11:03:21 11 triglycerides of at least 500 was actually done in the prior
11:03:24 12 art, right?

11:03:25 13 A In one or two people without much information on their
11:03:31 14 LDL? No, I would not say that that's true.

11:03:34 15 MR. KLEIN: Okay. Let's go to DDX 10.46.

11:03:34 16 BY MR. KLEIN:

11:03:41 17 Q And this was a slide that was used with Dr. Heinecke. I
11:03:45 18 don't know if you've seen this.

11:03:46 19 A I have seen it.

11:03:48 20 Q Okay. And for the record, there are five references on
11:03:51 21 this slide, DX 1532, page 5, DX 1550, page 32, DX 1546,
11:04:02 22 page 14, DX 1539, page 2, and DX 1537, page 23.

11:04:14 23 And you see on the screen there are references to
11:04:18 24 Hayashi from 1995, Saito from 1998, Takaku from 1991, and
11:04:23 25 Matsuzawa from 1991, and Nakamura from 1999.

11:04:28 1 **Do you see that?**

11:04:29 2 A **I do, counsel.**

11:04:30 3 Q **Okay. And Dr. Heinecke testified that each of these**

11:04:32 4 **studies contains at least one patient with triglycerides above**

11:04:36 5 **500.**

11:04:37 6 **Are you aware of that?**

11:04:38 7 A **I am.**

11:04:38 8 Q **Do you dispute Dr. Heinecke's testimony?**

11:04:41 9 A **I do.**

11:04:42 10 Q **So you dispute that these five references included at**

11:04:46 11 **least one patient above 500?**

11:04:49 12 A **Well, as you know, I strongly disputed that there was one**

11:04:52 13 **patient over 500 in Hayashi. In Saito, Nakamura, Matsuzawa,**

11:05:00 14 **Takaku, they do have one, and, in another case, three patients**

11:05:05 15 **over 500.**

11:05:07 16 **This does not constitute adequate evidence to me.**

11:05:09 17 Q **Okay. And let's -- let's unpack a little bit --**

11:05:15 18 A **Yeah.**

11:05:15 19 Q **-- to make sure I understand what you dispute.**

11:05:17 20 **You dispute that there's a patient above 500 in**

11:05:21 21 **Hayashi, correct?**

11:05:23 22 A **Yes.**

11:05:24 23 Q **Do you dispute that there was at least one patient**

11:05:26 24 **treated with pure EPA, who had triglycerides above 500 in the**

11:05:31 25 **Saito, Takaku, Matsuzawa, and Nakamura references?**

11:05:36 1 A I don't dispute that.

11:05:38 2 What I dispute is the reporting of the LDL. In two
11:05:42 3 of those four references they used the Friedewald equation to
11:05:46 4 estimate the LDL cholesterol which invalidates the analysis.

11:05:50 5 And Takaku also has missing data at two time points,
11:05:54 6 and he also notes that six patients had insufficient sample
11:05:59 7 with which to run measurements.

11:06:04 8 This is a very difficult set of papers to prove that
11:06:08 9 EPA was used in a convincing way in patients with
11:06:12 10 triglycerides over 500.

11:06:14 11 Q Okay. And, Doctor, it's important to listen carefully to
11:06:17 12 my question. I didn't ask anything about LDL. Okay?

11:06:20 13 A Okay.

11:06:21 14 Q So, to be clear, you don't dispute that at least one
11:06:24 15 patient was treated with pure EPA, and the patient had
11:06:28 16 triglycerides above 500 in Saito, Takaku, Matsuzawa, and
11:06:33 17 Nakamura; is that correct?

11:06:34 18 A I don't dispute that there were at least one patient in
11:06:41 19 those four papers with triglycerides over 500. Hayashi, yes.

11:06:47 20 Q Okay. Good.

11:06:49 21 Now -- and we'll talk about Hayashi -- before we do
11:06:54 22 so, on direct you testified there was nothing in the Epadel
11:06:56 23 label that would lead a skilled artisan that Epadel could be
11:07:00 24 used in patients above 500.

11:07:02 25 Do you remember that?

11:07:02 1 A Yes. It's too indistinct and nebulous to provide any
11:07:06 2 guidance on that issue.

11:07:07 3 MR. KLEIN: Okay. Let's go to DDX 10.127.

4 BY MR. KLEIN:

5 Q And, Doctor, this is DX 1528, which is the Epadel label.
6 And I'm focusing on pages 8 to 9.

7 You recall that there is a section called "Main
8 References" in the Epadel label, right?

9 A Yes, counsel.

10 Q Okay. And two of the references in the Epadel label are
11 Takaku, which is reference 8, and Matsuzawa, which is
12 reference 10, right?

13 A Yes.

14 Q And you agree that those two references included at least
15 one patient with triglycerides above 500, right?

11:07:49 16 A Without any information about what happened to -- okay.

11:07:52 17 Say it again, counsel. I'm so sorry.

11:07:55 18 Q You don't dispute that these two references, Takaku and
11:08:00 19 Matsuzawa, included at least one patient with triglycerides
11:08:03 20 above 500, correct?

11:08:05 21 A That's correct.

11:08:06 22 MR. KLEIN: Okay. Now let's go to DDX 10.47,
11:08:11 23 and this is DX 1542. In particular, I have page 4.

11:08:11 24 BY MR. KLEIN:

11:08:17 25 Q Do you recognize this as the Hayashi reference from 1995?

11:08:21 1 A I do, counsel.

11:08:23 2 Q All right. And you don't dispute that this is prior art,
11:08:27 3 correct?

11:08:27 4 A Oh, no.

11:08:27 5 Q Okay. And Hayashi says,

11:08:28 6 "The current study investigated the effects
11:08:31 7 of the ethylester of icosapent purified from fish
11:08:37 8 oils on plasma lipids" -- and then if you skip a
11:08:40 9 little bit, it says -- "in patients with familial
11:08:44 10 combined hyperlipidemia (FCH) showing phenotype" --
11:08:49 11 and among others, phenotype Type IV, right?

11:08:52 12 A Well, the problem is familial combined hyperlipidemia --
11:08:56 13 and they are referring to the Fredrickson system -- is Type
11:09:01 14 IIb, not IIa, not IV, it's IIb. So FCH is inappropriately
11:09:07 15 labeled Type IV here.

11:09:08 16 Q Okay. But you recognize the Type IV as the same label we
11:09:17 17 saw in the LIPITOR label, right?

11:09:21 18 A Uh --

11:09:21 19 Q The same -- the same category.

11:09:23 20 A Okay, it might be. I don't know.

11:09:30 21 Because if you're calling this a study of familial
11:09:34 22 combined hyperlipidemia, which is strictly IIb, by the
11:09:38 23 definition, IIa is familial hypercholesterolemia, and Type IV
11:09:45 24 is an elevation of VLDL.

11:09:50 25 So, no. I mean, I don't know if they followed,

11:09:54 1 rigorously the definitions because -- clearly, they didn't.

11:09:57 2 Q Okay. But the paper is reporting that it's investigating

11:10:00 3 the effects of EPA in patients who fall within Type IV of the

11:10:06 4 Fredrickson system. That's what the paper's saying.

11:10:09 5 A Well, I dispute it because they say "patients with

11:10:14 6 FCH" -- that is Type IIb alone.

11:10:18 7 Q Okay. But putting aside that maybe that was a typo, I

11:10:20 8 don't know, but --

11:10:21 9 A Yes. Would I put it aside?

11:10:23 10 Q No, no. I'm just saying it because I'm asking you a

11:10:25 11 question. Phenotype Type IV is under the Fredrickson system,

11:10:30 12 right?

11:10:30 13 A Yes.

11:10:31 14 Q And that is the phenotype type that we looked at in the

11:10:34 15 LIPITOR label and hour ago, right?

11:10:35 16 A Yes. But I have no indication that these people have any

11:10:39 17 clue as to what they're talking about when they're mixing FCH

11:10:43 18 with IIIa, IIb, and Type IV. I'm sorry, I cannot do it.

11:10:48 19 Q Okay. I'm just asking you what the paper is saying.

11:10:50 20 A I'm telling you what the paper is saying.

11:10:52 21 Q Okay. Phenotype Type IV can include patients above 500,

11:10:55 22 right?

11:10:55 23 A It's typically to 499.

11:10:57 24 Q Okay. But in the LIPITOR label we saw is goes above 500,

11:11:02 25 right?

11:11:02 1 A In the LIPITOR label, whatever standard they used. I
11:11:06 2 can't speak for that --

11:11:07 3 Q Okay.

11:11:08 4 A -- but they called it IV.

11:11:09 5 Q And just to be clear, the standard being used in the
11:11:13 6 LIPITOR label is the FDA standard, right?

11:11:16 7 A Did they say that?

11:11:18 8 Q FDA approved the LIPITOR label, correct?

11:11:21 9 A Yes, they did.

11:11:24 10 MR. KLEIN: All right. Let's go to DDX 10.49.

11:11:24 11 BY MR. KLEIN:

11:11:31 12 Q You are aware that Dr. Philip Lavin submitted a
11:11:35 13 declaration during prosecution saying that there was not even
11:11:39 14 one patient in the study, the Hayashi study, that would be
11:11:42 15 expected to have a triglyceride level of 450 milligrams per
11:11:47 16 deciliter or higher, correct?

11:11:50 17 A My understanding was he said no one would be over 500 --
11:11:56 18 s, this is directly quoted from the declaration of Dr. Lavin?

11:12:00 19 Q Yeah. And that's not really material to my question --

11:12:03 20 A Okay.

11:12:03 21 Q -- but you understand Dr. Lavin submitted a declaration
11:12:07 22 to the patent office saying no one over 500 was -- no patient
11:12:12 23 over 500 was in the Hayashi study, right?

11:12:15 24 A Yes, that I'm aware of.

11:12:16 25 Q And, for the record, we're looking at DX 1589, page 2.

11:12:20 1 A Could you please tell me which item that is.

11:12:25 2 Q No. I -- I'm just establishing that one point. I don't

11:12:29 3 think you need to look at the declaration to answer my next

11:12:32 4 question.

11:12:32 5 A Okay.

11:12:33 6 Q You didn't offer and independent opinion to corroborate

11:12:36 7 what Dr. Lavin said to the patent office, correct?

11:12:41 8 A That I provided the patent office with an independent

11:12:46 9 opinion?

11:12:46 10 Q No. You didn't offer an opinion -- Dr. Lavin is a

11:12:50 11 statistician, right?

11:12:51 12 A Yes.

11:12:51 13 Q You didn't offer any type of statistical opinion to

11:12:55 14 corroborate what Dr. Lavin told the patent office. That's

11:12:59 15 beyond your report and your testimony, correct?

11:13:00 16 A That's correct.

11:13:01 17 Q Okay. But you understand that Dr. Lavin later testified

11:13:05 18 at deposition?

11:13:06 19 A Yes.

11:13:07 20 MR. KLEIN: Okay. Let's go to DDX 10.50.

11:13:07 21 BY MR. KLEIN:

11:13:13 22 Q And this is the Lavin deposition transcript at 103 --

11:13:18 23 page 103, lines 8 to 21. And he was asked,

11:13:25 24 "Well, how could you have an average distance

11:13:28 25 from the mean of 233 and not have people above the

11:13:30 1 533?

11:13:31 2 "ANSWER: Well, let's put it this way, in

11:13:34 3 statistics it is possible. It is likely that you

11:13:38 4 have at least one or two observations above 533. It

11:13:42 5 isn't zero. Let's go on record there, it is not

11:13:47 6 zero. But because the standard deviation is

11:13:50 7 calculated from the numbers, you know that there must

11:13:53 8 be at least one subject that is greater than one

11:13:56 9 standard deviation to the plus.

11:13:58 10 "QUESTION: So given that, you would rewrite

11:14:02 11 paragraph 12?

11:14:02 12 "ANSWER: I would."

11:14:03 13 Have you seen that testimony before?

11:14:05 14 A I have.

11:14:06 15 Q Okay. And do you dispute Dr. Lavin's testimony that it

11:14:16 16 is likely that you will have at least one or two patients

11:14:19 17 above 533 in the Hayashi study?

11:14:21 18 A I don't agree with it.

11:14:23 19 When I look at the graphs in the paper -- and I

11:14:25 20 looked at all three very carefully, there are 25, 22 and 24

11:14:31 21 patients in that figure, there is no explanation as to what

11:14:35 22 happened to the missing data.

11:14:37 23 And, counsel, you use the word "typo" when I talked

11:14:40 24 about FCH in the Fredrickson classification. I strongly

11:14:47 25 suspect that that standard deviation is a typo. If the data

11:14:51 1 isn't there, I do not believe in imputing it, and, there's no
11:14:54 2 way to estimate it.

11:14:55 3 Q Okay. That's because you are a data driven physician and
11:14:59 4 researcher, right?

11:15:01 5 A Yeah. Where's the data? If there's someone over 500 in
11:15:05 6 that paper, no one can show me where that patient is.

11:15:08 7 MR. KLEIN: Okay. Now let's go back to DDX
11:15:12 8 10.51.

11:15:12 9 BY MR. KLEIN:

11:15:17 10 Q We're back at Hayashi, which was DX 1532.

11:15:24 11 And you don't dispute that the patients in the
11:15:27 12 Hayashi who were treated with EPA, showed a significant
11:15:31 13 reduction in triglycerides have 41 percent, right?

11:15:35 14 A No. That's in the paper.

11:15:37 15 Q Okay. And you don't dispute that EPA treatment had no
11:15:43 16 statistically significant effect on LDL-C as reported in
11:15:48 17 Hayashi, correct?

11:15:48 18 A I do not dispute that. It's in the table --

11:15:51 19 Q Okay.

11:15:52 20 A -- a statistically not significant 7 percent reduction.

11:15:57 21 MR. KLEIN: Let's go to DDX 10.52.

11:15:57 22 BY MR. KLEIN:

11:16:00 23 Q And in the Discussion and Conclusion section of
11:16:04 24 Hayashi -- this is DX 1532 at page 7 -- the authors concluded,
11:16:12 25 "Although the effects of fish oils on plasma

11:16:16 1 LDL-C and HDL-C are complex, judging from the present
11:16:20 2 study, purified EPA apparently has no deleterious
11:16:27 3 effect on plasma, LDL-C, or HDL-C in patients with
11:16:33 4 FCH," correct?
11:16:34 5 A Yes. Triglycerides less than 500.
11:16:37 6 Q Okay. And the authors did not limit this conclusion in
11:16:39 7 any way, right?
11:16:40 8 A Well, they have to limit it to the data they have and
11:16:43 9 they have no one with triglycerides over 500.
11:16:45 10 Q The authors did not say we would expect LDL-C spikes once
11:16:50 11 you get above 500.
11:16:51 12 A Well, that just might mean they don't know what to
11:17:00 13 expect.
11:17:03 14 MR. KLEIN: All right. Let's go to DDX 10.588.
11:17:03 15 BY MR. KLEIN:
11:17:11 16 Q And I'm changing topics. I want to go back to your
11:17:14 17 testimony that Lovaza was -- had been prescribed with statins,
11:17:19 18 okay, to orient you.
11:17:20 19 A Thank you.
11:17:20 20 Q All right. So on the screen is DX 1578, page -- Table 2,
11:17:27 21 page 1.
11:17:28 22 Do you recognize this as the Lovaza label?
11:17:30 23 A Yes.
11:17:30 24 Q Okay. And, again, the Lovaza label talks about how using
11:17:41 25 the drug to reduce very high triglycerides may result in LDL-C

11:17:47 1 **elevations in some individuals, right?**

11:17:49 2 A **Yes.**

11:17:50 3 Q **Now, to be clear, the Lovaza label isn't saying that the drug always causes LDL-C increases, right?**

11:17:56 5 A **No drug always does one thing, and I think we've established that. So, no, you're not going to see a uniform response. There will be a distribution of responses.**

11:18:06 8 Q **Right -- except for cyanide, right?**

11:18:09 9 A **Yeah. There's one response to that.**

11:18:11 10 MR. KLEIN: **Okay. All right. So let's go to DDX 10.59.**

11:18:15 12 **BY MR. KLEIN:**

11:18:17 13 Q **This is Table 1 from the Lovaza label -- still DX 1578, page 1 -- and this table discusses Lovaza when used with simvastatin, right?**

11:18:29 16 A **Yes.**

11:18:30 17 Q **And simvastatin is, obviously, a statin, correct?**

11:18:33 18 A **Yes.**

11:18:34 19 Q **Okay. And this teaches that when Lovaza is used with simvastatin, apo B is reduced by 4.2 percent, right?**

11:18:43 21 A **Yes.**

11:18:43 22 Q **Okay. And when Lovaza is used with simvastatin, there's barely any LDL-C increase, correct?**

11:18:50 24 A **Yes.**

11:18:51 25 Q **And that's -- and it says .7 percent, but that's not**

11:18:54 1 **clinically significant, right?**

11:18:56 2 A **We'll take that as zero.**

11:18:59 3 MR. KLEIN: Okay. Let's go to DDX 10.60. This
11:19:04 4 **is DX 2005, page 8.**

11:19:04 5 **BY MR. KLEIN:**

11:19:08 6 Q **Do you recognize this as the Zocor simvastatin
11:19:12 7 indication?**

11:19:15 8 A **Yes.**

11:19:15 9 MR. KLEIN: I'll move into evidence DX 2005.

11:19:19 10 MR. ELIKAN: No objection.

11:19:19 11 THE COURT: 2005 is admitted.

11:19:19 12 (Defendants' Exhibit 2005 received in
11:19:22 13 **evidence.)**

11:19:22 13 **BY MR. KLEIN:**

11:19:22 14 Q **Simvastatin was approved to reduce elevated total
11:19:27 15 cholesterol, LDL-C, apo B, among other things, right?**

11:19:31 16 A **Yes.**

11:19:31 17 Q **Okay. Now focusing back on the Lovaza, you prescribed
11:19:38 18 that drug frequently before March 2008, right?**

11:19:42 19 A **Yes.**

11:19:42 20 Q **Okay. And when you did so, you knew that the drug could
11:19:46 21 increase LDL-C in some patients, right?**

11:19:49 22 A **Certainly.**

11:19:50 23 Q **Okay. And it didn't always increase LDL-C in your
11:19:55 24 patients, right?**

11:19:56 25 A **I would say it usually did. But, there's no blanket**

11:19:59 1 **statement.**

11:19:59 2 Q Okay. And when you prescribed Lovaza, you didn't intend

11:20:03 3 for your patient's LDL-C to increase, right?

11:20:06 4 A No. I kept a close eye on that.

11:20:08 5 Q Right. You hoped it wouldn't increase, right?

11:20:11 6 A Yes.

11:20:11 7 Q And if it did increase, you would then prescribe a

11:20:14 8 lipid-altering therapy, like a statin, correct?

11:20:18 9 A Yes. I was in attack mode then.

11:20:20 10 Q Okay. And a skilled artisan would know from the Lovaza

11:20:23 11 label, that taking 4 grams of Lovaza with a statin could

11:20:27 12 prevent LDL-C increases in patients with very high

11:20:31 13 triglycerides, right?

11:20:32 14 A It could depending on the dose, depending upon the statin

11:20:37 15 potency. It could. I would qualify it with the word "could."

11:20:41 16 Q And a skilled artisan, as of March 2008, would understand

11:20:44 17 that if a patient is experiencing LDL-C increases because of

11:20:48 18 Lovaza, a statin could be added, right?

11:20:50 19 A Yes.

11:20:54 20 Q And the label itself makes that clear, right?

11:20:57 21 A Yes.

11:20:57 22 Q Okay. And as of March 2008, it was known that Lovaza

11:21:00 23 could be safely administered with statins, correct?

11:21:03 24 A Yes.

11:21:04 25 MR. KLEIN: Let's go to DDX 10.61.

11:21:04 1 BY MR. KLEIN:

11:21:09 2 Q I will represent to you that this comes from Amarin's
11:21:13 3 validity contentions, and it's DX 1953, page 233.

11:21:20 4 And Amarin -- these are -- this is something that
11:21:22 5 Amarin created for this case -- said that,

11:21:25 6 "The rise in LDL-C was often offset by
11:21:29 7 concurrent treatment with statins. The safety and
11:21:33 8 efficacy of using prescription Omega-3 in combination
11:21:36 9 with a statin has been well-established."

11:21:38 10 Do you see that?

11:21:39 11 A I do.

11:21:40 12 Q That's an accurate statement, correct?

11:21:42 13 A It is accurate.

11:21:43 14 Q And, in fact, Lovaza was administered safely with statins
11:21:50 15 all the time before March 2008, right?

11:21:52 16 A Yes. It could be safely co-administered.

11:21:55 17 MR. KLEIN: Okay. Let's go to DDX 10.62.

11:21:55 18 BY MR. KLEIN:

11:21:59 19 Q Now, this is DX 1502, page 22. You recognize this as
11:22:05 20 claims 13 and 14 of the '715 patent, right?

11:22:09 21 A Yes.

11:22:09 22 Q And I'm including claim 13 because claim 14 depends on
11:22:15 23 claim 13, you understand that?

11:22:16 24 A Yes.

11:22:17 25 Q Okay. And claim 13 includes a limitation "Who does not

11:22:21 1 receive a concurrent lipid-altering therapy."

11:22:25 2 Do you see that?

11:22:26 3 A Yes.

11:22:26 4 Q Okay. And the claim also requires that there be "no
11:22:30 5 statistically significant increase in LDL-C or apo B," right?

11:22:35 6 A Yes.

11:22:35 7 Q Okay. I want to unpack these limitations to make it
11:22:39 8 clear how they relate to one another. Okay?

11:22:42 9 A Okay.

11:22:43 10 Q Now, a statin is, obviously, an example of a concurrent
11:22:47 11 lipid-altering therapy, right?

11:22:49 12 A Yes.

11:22:49 13 Q And as we discussed, statins can reduce LDL-C and apo B.
11:22:54 14 They're approved for that, right?

11:22:56 15 A Yes.

11:22:56 16 Q Okay. And so this limitation requiring that the patient
11:22:59 17 does not receive a concurrent lipid-altering therapy, makes it
11:23:05 18 clear that the pure EPA is having no effect on LDL-C or apo B.

11:23:10 19 Is that how you understand it?

11:23:11 20 A Yes.

11:23:11 21 Q Right.

11:23:13 22 A Yeah. So the apo B would, on average, go down; the LDL
11:23:18 23 would, on average, be neutral.

11:23:19 24 Q Right.

11:23:20 25 Now, by March 2008, it was known that EPA could be

11:23:23 1 used with a statin, correct?

11:23:28 2 A Yes.

11:23:29 3 MR. KLEIN: Okay. Let's go to DDX 10.62. This
11:23:35 4 is DX 1539.

11:23:35 5 BY MR. KLEIN:

11:23:37 6 Q Do you recognize this as the Nakamura reference?

11:23:40 7 A Yes.

11:23:40 8 Q And page 1, in Nakamura, used 900 to 18 [sic] milligrams
11:23:49 9 per day of EPA to patients with hyperlipidemia who had been
11:23:55 10 treated with HMG-CoA reductase inhibitors for 30 plus months,
11:24:01 11 right?

11:24:01 12 A Yes.

11:24:01 13 Q Okay. And just so we're clear, "HMG-CoA reductase
11:24:06 14 inhibitors" is a fancy word for statin, right?

11:24:16 15 A Yeah. Hydroxymethylglutaryl coenzyme A reductase
11:24:16 16 inhibitors.

11:24:16 17 Q I was trying to avoid that.

11:24:23 18 A Yes, counsel, HMG-CoA.

11:24:23 19 Q Okay. And, by the way, Nakamura is one of those
11:24:26 20 references that included a patient above 500, right?

11:24:29 21 A Can you show me where? Let me see that.

11:24:32 22 Show me the paper, which --

11:24:34 23 Q Well --

11:24:35 24 A I just -- these papers are starting to float around in my
11:24:39 25 head.

11:24:39 1 Q Why don't we go back -- it might be easier to go back
11:24:43 2 to --

11:24:55 3 THE COURT: Would it help to go back to the
11:24:57 4 chart where all the papers are listed?

11:24:59 5 MR. KLEIN: I'm just going to go back to
11:25:03 6 Dr. Heinecke's chart because I don't think it's disputed.

11:25:07 7 DDX 10.46, please.

11:25:12 8 THE WITNESS: Nakamura -- okay. Thank you.

11:25:15 9 Thank you, counsel.

11:25:16 10 BY MR. KLEIN:

11:25:16 11 Q All right. And so it was known by March 2008, that pure
11:25:20 12 EPA could be given with statins, even in patients above 500,
11:25:25 13 right?

11:25:25 14 A Are you saying in Nakamura based on one patient, or based
11:25:32 15 on the label?

11:25:33 16 Q I'm saying based on the fact that pure EPA was given to
11:25:36 17 at least one patient above 500 with a statin, it was known
11:25:42 18 that pure EPA could be given to patients above 500 with a
11:25:46 19 statin, right?

11:25:47 20 A If you take one patient seriously, okay. Yeah.

11:25:51 21 Q Okay. It was actually done in the art, in other words,
11:25:57 22 even if it's one patient --

11:25:58 23 A One patient. Yes.

11:26:00 24 Q Now -- and we'll talk about JELIS later, but JELIS
11:26:03 25 involved pure EPA with a statin as well, right?

11:26:06 1 A Yes.

11:26:06 2 MR. KLEIN: Okay. Let's go back to DDX10.65. I

11:26:12 3 want to go back to claim 14 of the '715 patent. Again, this

11:26:17 4 is DX 1502, page 22.

11:26:17 5 BY MR. KLEIN:

11:26:21 6 Q And so this claim expressly excludes use of a concurrent

11:26:25 7 lipid-altering therapy, right?

11:26:27 8 A Yes.

11:26:27 9 Q And so -- and that's because a skilled artisan would know

11:26:31 10 that a patient taking pure EPA with a statin will not have an

11:26:36 11 LDL-C increase because statins reduce LDL-C, right?

11:26:41 12 A Depending upon the magnitude of the LDL elevation, yeah.

11:26:45 13 So with that one qualification, the statin can neutralize that

11:26:50 14 LDL elevation, but it depends on the baseline triglyceride.

11:26:54 15 Yes.

11:26:54 16 Q Right. So a skilled artisan, in 2008, would understand

11:26:58 17 that if you give pure EPA with a statin, you're not going to

11:27:01 18 have a LDL-C increase, right?

11:27:03 19 A Well, you won't have as much of an LDL increase, or

11:27:07 20 perhaps you won't increase LDL.

11:27:09 21 Q Okay. And the same thing with apo B, a skilled artisan,

11:27:12 22 in March 2008, would understand that if you give a pure EPA

11:27:15 23 with a statin, you're likely to have an apo B decrease,

11:27:22 24 correct?

11:27:22 25 A Yes, that would be logical.

11:27:24 1 Q Okay. And that would be true whether the triglyceride
11:27:26 2 level is 400 or 550, right?
11:27:29 3 A Again, no blanket statements. But, the odds are yes.
11:27:33 4 Q All right. So going back to claim 14, what claim 14 of
11:27:44 5 the '715 patent is doing is it's avoiding this known method of
11:27:51 6 using pure EPA with a statin to reduce LDL-C and apo B by
11:27:56 7 saying the patient cannot receive a concurrent lipid-altering
11:27:59 8 therapy.

11:28:00 9 Is that your understanding?

11:28:01 10 A Repeat that, please.

11:28:04 11 Q Okay. I'll try.

11:28:04 12 Claim 14 is -- the point of claim 14 is to carve out
11:28:09 13 the known use of pure EPA with a statin to reduce not only
11:28:16 14 triglycerides, but also LDL-C and apo B, by expressly saying
11:28:22 15 the patient can't take a concurrent lipid-altering therapy,
11:28:28 16 right?

11:28:28 17 A Okay. Well, let me unpack that a little bit.

11:28:30 18 Q Okay.

11:28:30 19 A So, basically, they're saying that if you use 4 grams of
11:28:36 20 purified EPA, 96 percent pure, you will induce a statistically
11:28:43 21 significant reduction in triglycerides without affecting the
11:28:48 22 statistically significant increase of apo B.

11:28:51 23 Q Okay.

11:28:51 24 A That's my reading.

11:28:53 25 Q All right. Let me try to simplify it a little bit.

11:28:56 1 **We talked about how pure EPA could be used with**
11:29:00 2 **statins to reduce apo B and LDL-C, right?**

11:29:05 3 A **Yes.**

11:29:05 4 Q **And that was known in March 2008?**

11:29:07 5 A **Yes.**

11:29:07 6 Q **And so what this claim, claim 14 of the '715 patent is**
11:29:11 7 **doing, is saying we're only claiming the use of EPA without a**
11:29:16 8 **statin, and that pure EPA, itself, has to have no LDL-C**
11:29:21 9 **increase and apo B reduction.**

11:29:24 10 **Is that your understanding?**

11:29:26 11 A **Yes.**

11:29:26 12 Q **Okay. Now, to be clear, the prior art also taught that**
11:29:31 13 **pure EPA, even 4 grams pure EPA, could be used without a**
11:29:35 14 **statin to reduce triglycerides, right?**

11:29:37 15 A **Yes.**

11:29:38 16 Q **And that's the Mori reference?**

11:29:39 17 A **No. No, no, no. No, no, no. Correct that.**

11:29:43 18 **Repeat that question, please.**

11:29:45 19 Q **I don't -- let's go to DDX 10.66 because I don't think**
11:29:49 20 **this will be disputed. So maybe you misheard my --**

11:29:49 21 A **Okay. Yeah.**

11:29:52 22 Q **This is DX 1538, pages 2 and 3.**

11:29:56 23 **Do you recognize this as coming from the Mori 2000**
11:29:59 24 **reference?**

11:29:59 25 A **Yes, counsel.**

11:30:00 1 Q And Mori used 4 grams pure EPA without a lipid-lowering
11:30:04 2 drug, correct?

11:30:05 3 A Yes.

11:30:05 4 Q Okay. That's all I was asking.

11:30:06 5 A Yes.

11:30:07 6 Q Okay. So there were clinical studies in the prior art
11:30:10 7 that discuss using pure EPA to reduce triglycerides with and
11:30:14 8 without a statin, right?

11:30:16 9 A Yes, below 500.

11:30:18 10 Q Okay. Now, it would have been obvious to a skilled
11:30:25 11 artisan, before March 2008, to give a patient pure EPA, either
11:30:30 12 with or without a statin below 500, right?

11:30:35 13 A Yes, it -- yes. Yes.

11:30:39 14 Q Okay. And you didn't provide any opinion disputing that
11:30:44 15 it would be obvious to use pure EPA without a statin, right?

11:30:51 16 A I -- that I didn't dispute that you could use pure EPA
11:30:55 17 without a statin?

11:30:57 18 Q Well, let's go back to the claim, which is DDX 10.62.

11:31:30 19 A Thank you.

11:31:31 20 Q All right. So with regard to the limitation "who does
11:31:33 21 not receive a concurrent lipid-altering therapy," you're not
11:31:36 22 disputing that it would be obvious to use pure EPA without a
11:31:40 23 concurrent lipid-altering therapy, right?

11:31:44 24 A Am I disputing claim 13?

11:31:46 25 Q No, not just -- I'm just focusing on that one limitation.

11:31:50 1 You're not disputing that it would have been obvious
11:31:52 2 to skilled artisan, in March 2008, to use pure EPA without a
11:31:58 3 concurrent lipid-altering therapy to reduce triglycerides,
11:32:02 4 correct?

11:32:03 5 A Based on this claim, no.

11:32:04 6 Q All right. Now --

11:32:05 7 A You mean in patients with triglycerides of 500 to 1500?

11:32:10 8 Q Well, I -- well, I know you dispute above 500, right, so
11:32:13 9 I didn't ask the question above 500.

11:32:16 10 A Okay.

11:32:17 11 MR. KLEIN: Okay. To be fair.

11:32:17 12 So let's go to DDX 10.67. This is another claim
11:32:26 13 in the patent that's being asserted, claim -- '677, claim 8,
11:32:30 14 and it's DX 1504, pages 21 and 22.

11:32:30 15 BY MR. KLEIN:

11:32:34 16 Q Do you see that?

11:32:35 17 A Yes.

11:32:35 18 Q And you understand that claim 8 depends on claim 1?

11:32:39 19 A Yes.

11:32:40 20 Q Okay. And claim 8 requires a reduction in apo B.

11:32:44 21 Do you see that?

11:32:45 22 A Yes.

11:32:45 23 Q Claim 1 requires use of the drug without substantially
11:32:50 24 increasing LDL-C, right?

11:32:52 25 A Yes.

11:32:53 1 Q But claim 8 of the '677 patent does not exclude using a
11:32:59 2 concurrent lipid-altering therapy, correct?

11:33:03 3 A A method of claim1 comprising administering to the
11:33:08 4 subject of 4 grams --

11:33:08 5 THE COURT: Are you reading it to yourself?

11:33:09 6 If you want to read it, just read it. Don't
11:33:11 7 read in out loud because, otherwise, you have to slow down if
11:33:15 8 you want to read it out loud.

11:33:17 9 THE WITNESS: Thank you. Thank you, Your Honor.

11:33:23 10 (Witness reviews document.)

11:33:25 11 Okay, counsel. So your question is?

11:33:28 12 BY MR. KLEIN:

11:33:28 13 Q Okay. Remember we looked at the limitation in one of the
11:33:31 14 claims that had -- that says you must exclude a concurrent
11:33:36 15 lipid-altering therapy?

11:33:37 16 A That you must exclude it?

11:33:39 17 Q Yeah. Remember, we just looked at that? It was -- do
11:33:43 18 you want me to put the claim back on?

11:33:45 19 A If you would, please.

11:33:46 20 MR. KLEIN: Let's go to DDX 10.62 again.

11:33:49 21 THE WITNESS: I just don't recall that "you must
11:33:50 22 exclude it."

11:33:50 23 BY MR. KLEIN:

11:33:51 24 Q Okay, 62.

11:33:59 25 The first highlighting, remember, we talked about

11:34:02 1 that limitation "who does not receive a concurrent
11:34:04 2 lipid-altering therapy"?

11:34:05 3 A Yes.

11:34:06 4 Q And you understand that that limitation in claim 14 means
11:34:11 5 the claim doesn't cover situations where, for example, 4 grams
11:34:15 6 pure EPA is with a statin.

11:34:20 7 A That it, necessarily, excludes a statin?

11:34:25 8 Q Well, I mean the -- I'm not -- I'm not trying to trick
11:34:29 9 you here.

11:34:30 10 The limitation in claim 13 set a requirement of this
11:34:37 11 patent claim is that the patient not received a concurrent
11:34:39 12 lipid-altering therapy, right?

11:34:41 13 A It states "who does not receive a concurrent
11:34:44 14 lipid-altering therapy," yes.

11:34:46 15 Q And so your understanding is to practice claim 14 of the
11:34:49 16 '715 patent, you can't give the patient a statin in addition
11:34:54 17 to the EPA.

11:34:55 18 Do you understand that's how that claim works?

11:34:57 19 A So that you can't?

11:34:58 20 Q You can't, because the claim says the "patient does not
11:35:01 21 receive a concurrent lipid-altering therapy."

11:35:04 22 A But it doesn't say that you can't receive a concurrent --

11:35:07 23 THE COURT: Perhaps, Mr. Klein, you could
11:35:09 24 rephrase your question and say assuming that --

11:35:09 25 MR. KLEIN: Okay.

11:35:12 1 THE COURT: -- you have to accept this premise.

11:35:14 2 BY MR. KLEIN:

11:35:15 3 Q Now, Doctor, I know you're not a patent lawyer, okay,

11:35:17 4 so --

11:35:17 5 A Oh, I am not a patent lawyer.

11:35:19 6 Q All right. So do you have general understanding that

11:35:22 7 some of the asserted claims in this case allow for the use of

11:35:25 8 a statin with icosapent, and some say you can't take icosapent

11:35:32 9 with a statin?

11:35:33 10 A Yes.

11:35:33 11 Q Okay. And do you have general understanding that seven

11:35:36 12 of the ten claims asserted in this case allow for the use of a

11:35:41 13 statin with icosapent?

11:35:42 14 A Yes.

11:35:43 15 Q Okay. And so those claims that allow for the use of a

11:35:53 16 statin would include using 4 grams pure icosapent with a

11:35:59 17 statin to -- and not have an LDL-C increase.

11:36:05 18 You understand that, right?

11:36:06 19 A Yes.

11:36:06 20 Q Okay. And those claims would also allow the use of

11:36:10 21 4 grams pure EPA -- again above 500 -- with a statin, to

11:36:16 22 reduce apo B, right?

11:36:18 23 A That would be one manifestation of the statin use would

11:36:22 24 be to help reduce apo B.

11:36:25 25 MR. KLEIN: Okay. Thank you.

11:36:26 1 Now, I want to switch gears a little bit here
11:36:31 2 and talk about something you discussed on direct.
11:36:33 3 Mr. Gross, can you put up PX 989.
11:36:33 4 BY MR. KLEIN:
11:36:39 5 Q Do you recognize PX 989 as the ATP III guidelines?
11:36:44 6 A Yes, counsel.
11:36:45 7 MR. KLEIN: Okay. Let's go to page 90 of the
11:36:47 8 exhibit. Hold on. I must have the wrong -- 190, I'm sorry.
11:37:03 9 Okay. Can you highlight the chart in the upper
11:37:05 10 right.
11:37:05 11 BY MR. KLEIN:
11:37:08 12 Q And do you remember talking about this chart on direct?
11:37:10 13 A Yes.
11:37:10 14 Q All right. And you talked about two genetic causes for
11:37:15 15 very high triglycerides on the bottom right of this table,
11:37:19 16 right?
11:37:19 17 A Yes.
11:37:19 18 Q And they are familial lipoprotein lipase deficiency, and
11:37:25 19 familial apolipoprotein C-II deficiency, right?
11:37:31 20 A That was pretty good.
11:37:32 21 Q And those are the only two genetic causes of very high
11:37:37 22 triglycerides listed in Table 7.2-1 of the ATP III guidelines,
11:37:43 23 right?
11:37:43 24 A In the Table; there's a third in the text.
11:37:45 25 Q Okay. But the text also talks about how these two -- I

11:37:50 1 **won't repeat them again -- are the most frequently reported,**
11:37:54 2 **common genetic defects that cause very high triglycerides,**
11:37:57 3 **right?**

11:37:57 4 | A Yes.

11:37:58 5 Q Okay. And to be clear, the first bullet says usually --
11:38:04 6 the first bullet under very high triglycerides, says "usually
11:38:08 7 combined causes," same for high triglycerides, right?

11:38:11 8 A Yes, it states that.

11:38:12 9 Q Okay. And though -- and that's referring back up to all
11:38:16 10 the other causes of borderline high triglycerides and high
11:38:21 11 triglycerides, right?

11:38:21 12 A Some of them can be included, yes.

11:38:24 13 Q And so what this chart is teaching a skilled artisan is
11:38:29 14 that, you know, some patients can have these genetic defects,
11:38:34 15 and others may have all these other potential causes, right?

11:38:37 16 A It could be a mixed picture, yes. But, generally, it's
11:38:44 17 genetic. But, yeah, there could be combinations of causes.

11:38:47 18 O Okay. And you talked about the MARINE study, right?

11:38:49 19 A Yes ..

11:38:50 20 Q Okay. Now, the MARINE study focused on all these other
11:38:55 21 causes, and not those two genetic causes we talked about,
11:38:59 22 right?

11:39:00 23 A Well, I'm not sure that that's right.

11:39:06 24 Where does MARINE state that it's due to all these
11:39:09 25 other causes?

11:39:10 1 MR. KLEIN: All right. Let's go to DX 1694.

11:39:10 2 BY MR. KLEIN:

11:39:16 3 Q Do you recognize DX 1694 as the Clinical Study Report for

11:39:21 4 MARINE?

11:39:21 5 A Yes, counsel. I'm just pulling up the paper here.

11:39:24 6 Q Sure. Let me know when you have it.

11:39:28 7 A Doesn't look like it's in this binder, but we can look at

11:39:32 8 the pages.

11:39:33 9 MR. KLEIN: Okay. Yeah. Let's go to pages 31

11:39:36 10 and 32.

11:39:39 11 Okay. You see -- let's highlight 9.3.2.

11:39:39 12 BY MR. KLEIN:

11:39:48 13 Q And do you see at the top it talks about "exclusion

11:39:52 14 criteria" for the study?

11:39:53 15 A Yes.

11:39:53 16 Q It says,

11:39:55 17 "Patients were to be excluded from

11:39:56 18 participation in the study if any of the following

11:39:59 19 criteria apply..."

11:40:01 20 Do you see that?

11:40:01 21 A I do.

11:40:02 22 MR. KLEIN: Okay. Let's close that and go to

11:40:04 23 paragraph 11 on the next page.

11:40:08 24 This is, for the record, DX 1694, at page 32.

11:40:08 25

11:40:08 1 BY MR. KLEIN:

11:40:19 2 Q Okay. And one of the exclusion criteria is known
11:40:23 3 familial lipoprotein lipase impairment or deficiency,
11:40:29 4 Fredrickson Type I, apolipoprotein C-II deficiency, and also
11:40:37 5 familial --

11:40:38 6 A Dysbetalipoproteinemia -- and court reporter, I'll spell
11:40:38 7 that for you --

11:40:38 8 COURT REPORTER: I have it.

11:40:38 9 THE WITNESS: Okay. Thank you.

11:40:38 10 BY MR. KLEIN:

11:40:46 11 Q Okay. Fredrickson Type III, correct?

11:40:46 12 A Yes.

11:40:47 13 Q Okay. And so you understand that patients with these
11:40:51 14 genetic conditions for severe hypertriglyceridemia were
11:40:54 15 excluded from the MARINE study?

11:40:56 16 A Based on the criteria, yes.

11:41:01 17 Q Now, let's turn to unmet need. You talked about that on
11:41:10 18 direct, right?

11:41:10 19 A Yes.

11:41:10 20 Q That was one of the bases on which the examiner allowed
11:41:17 21 the patents, right?

11:41:18 22 A Yes.

11:41:19 23 Q And in your opinion, Lovaza is one of the closest prior
11:41:23 24 art to Vascepa, right?

11:41:24 25 A Yes.

11:41:24 1 Q Or the claims, really.

11:41:25 2 A Yes.

11:41:26 3 Q And there's no dispute that Lovaza and Vascepa are

11:41:30 4 indicated for the same method of treatment, correct?

11:41:33 5 A Yes. They both have indications for severe

11:41:36 6 hypertriglyceridemia.

11:41:37 7 Q Okay. And some background, Lovaza was a very successful

11:41:41 8 drug, right?

11:41:42 9 A Yes.

11:41:42 10 Q It was a blockbuster, more than a billion dollars per

11:41:48 11 year, right?

11:41:48 12 A That I don't know. But, yes, it was widely used.

11:41:51 13 Q Okay. And the LDL-C side effect of Lovaza did not stop

11:41:55 14 doctors from prescribing the drug all the time, right?

11:41:58 15 A It's the best we had.

11:42:00 16 Q Including you; you prescribed it many, many times, right?

11:42:03 17 A I did.

11:42:04 18 Q And as discussed, the FDA-approved label allowed for the

11:42:08 19 use of Lovaza with a statin, if there were LDL-C issues,

11:42:12 20 right?

11:42:12 21 A You could. Yes.

11:42:13 22 Q And a skilled artisan, as of March 2008, would understand

11:42:16 23 that if a patient experiences LDL-C increase from Lovaza, the

11:42:21 24 statin could be added to address that side effect, right?

11:42:24 25 A It could.

11:42:25 1 Q Yeah. And you served on the GSK Speakers Bureau for
11:42:29 2 Lovaza, right?
11:42:30 3 A I did.
11:42:30 4 Q And when talking to doctors about Lovaza you discussed
11:42:33 5 the LDL-C side effect, right?
11:42:35 6 A Of course.
11:42:36 7 Q And you told doctors to add an LDL lowering agent, such
11:42:40 8 as a statin, to address LDL effects from Lovaza, right?
11:42:44 9 A Yes.
11:42:45 10 Q And you told doctors that, in your experience, using a
11:42:49 11 statin helps reduce the LDL-C effects from Lovaza, right?
11:42:52 12 A Yes.
11:42:53 13 Q And I think you testified earlier that the vast majority
11:42:58 14 of patients who take Lovaza with a statin are able to tolerate
11:43:02 15 the statin, correct?
11:43:03 16 A No, I did not say that the vast majority of patients who
11:43:07 17 take a statin with Lovaza have no problem tolerating the
11:43:10 18 statin.
11:43:10 19 Q Okay.
11:43:11 20 A What I did say in testimony yesterday -- and I think I
11:43:14 21 reiterate that today -- was that you could use a statin, but
11:43:19 22 there are limitations.
11:43:21 23 I mean, obviously, we would love to be able to use
11:43:24 24 high dose high potency statins for everybody who needs them,
11:43:28 25 but not everyone can tolerate them. Some people don't

11:43:31 1 tolerate statins at all, unfortunately. Some people only
11:43:35 2 tolerate lower doses.

11:43:37 3 And my other caveat there was that if the LDL
11:43:40 4 elevation was particularly severe, you might have to burn
11:43:43 5 all of your LDL reducing capacity with a high dose high potency
11:43:43 6 statin just to get them back to baseline.

11:43:50 7 But, yes, some patients you could get that LDL down
11:43:53 8 just fine but not everyone.

11:43:55 9 Q Okay. But you found that the use of statins by your
11:43:58 10 patients taking Lovaza was typically well-tolerated, correct?

11:44:01 11 A It was typically well-tolerated.

11:44:03 12 Q Okay. And you did not see situations where Lovaza's
11:44:08 13 patient's LDL-C increased to such a degree that the patient
11:44:12 14 could not use the medication anymore, right?

11:44:14 15 A Well, okay. If the patient's LDL increase was severe, I
11:44:20 16 might have to use two drugs to lower that LDL, like statin
11:44:24 17 and, by way of example, acetamide. So, it would complicate
11:44:29 18 the management of the patient. It would increase the expense
11:44:32 19 of managing the LDL elevation.

11:44:34 20 But we did what we could to control it.

11:44:37 21 Q Now, in the large majority of cases you saw no instance
11:44:41 22 where patient's LDL-C increased to such a degree that you
11:44:46 23 could not use the medication anymore; is that fair?

11:44:49 24 A Well, again, it depends if the patient tolerated the
11:44:53 25 statin, tolerated LDL-lowering medication. Again, I'm not

11:44:57 1 going to make a blanket statement, but generally I was able to
11:45:01 2 deal with it. I'll say that.

11:45:09 3 MR. KLEIN: Okay. Let's talk about REDUCE-IT.

11:45:15 4 Let's go to DDX 10.76.

11:45:15 5 BY MR. KLEIN:

11:45:20 6 Q And you'll probably recognize this as PDX 6.23 from your
11:45:27 7 direct, right?

11:45:28 8 A Yes.

11:45:28 9 Q And you discussed whether REDUCE-IT has a nexus to the
11:45:31 10 asserted claims, right?

11:45:33 11 A Yes.

11:45:33 12 Q Now, REDUCE-IT focused on patients with triglycerides
11:45:36 13 below 500, right?

11:45:38 14 A Yes.

11:45:38 15 Q Okay. And you understand that none of the patent claims
11:45:42 16 at issue in this case have a limitation with regard to
11:45:44 17 reducing cardiovascular risk?

11:45:47 18 A Yes.

11:45:47 19 Q And that none of the patent claims require patients to
11:45:53 20 have any cardiovascular risk factors, right?

11:45:55 21 A Well, having hypertriglyceridemia is a risk factor.

11:45:59 22 Q Okay. Well, aside from severe high triglycerides,
11:46:03 23 there's no other risk factor required by the patents related
11:46:07 24 to cardiovascular issues, correct?

11:46:08 25 A That's correct.

11:46:09 1 Q Okay. And you're not offering any opinion related to
11:46:14 2 this rebuttable presumption that's on the screen, right?

11:46:18 3 A No.

11:46:18 4 Q Okay. But you do understand that Amarin has separate
11:46:22 5 patents covering the method used in the REDUCE-IT study,
11:46:29 6 correct?

11:46:29 7 A Yes.

11:46:30 8 Q And you understand that those patents are not being
11:46:32 9 asserted in this case?

11:46:33 10 A Yes.

11:46:34 11 Q All right. And, of course, you understand the claims in
11:46:38 12 this case focus on treating patients for at least 12 weeks?

11:46:41 13 A Yes.

11:46:42 14 Q And you didn't offer any opinion that REDUCE-IT showed
11:46:45 15 any cardiovascular benefit with -- as of 12 weeks, right?

11:46:50 16 A That's correct, with the caveat that by taking it for
11:46:55 17 12 weeks, you would be altering that patient's lipid profile,
11:46:59 18 inflammatory mediator profile, in ways that would be expected
11:47:03 19 to yield cardiovascular benefit over time.

11:47:06 20 Q But understand the patents cover situations where a
11:47:09 21 patient takes Vascepa for just four months, then stops, right?

11:47:16 22 A I must say I can't think of a patient that I started on
11:47:20 23 Vascepa and stopped in four months.

11:47:21 24 Q Well, I mean -- and I don't want to get into issues of
11:47:24 25 infringement. That's not my purpose here.

11:47:26 1 You understand that there -- that the claims cover a
11:47:31 2 situation where the drug could be taken for four months and
11:47:36 3 stopped, and that's within the scope of the claims.

11:47:38 4 You understand that, right?

11:47:39 5 A Yes.

11:47:39 6 Q Okay. But you're not offering an opinion that a patient
11:47:43 7 who takes the drug for four months and stops is going to have
11:47:46 8 the cardiovascular benefits received in the REDUCE-IT trial,
11:47:50 9 right?

11:47:50 10 A Well, it takes time to accrue the benefit, and if you
11:47:54 11 stop it at four months, the four months certainly laid the
11:47:58 12 foundation to approach a period of time where you would expect
11:48:01 13 benefit. But if you stop it at four months, then you're going
11:48:05 14 to lose that benefit.

11:48:10 15 Q And all the patients in REDUCE-IT were taking statins,
11:48:13 16 right?

11:48:13 17 A Yes.

11:48:19 18 Q And -- so 100 percent, right?

11:48:20 19 A Yes.

11:48:20 20 Q And 25 percent of the patients in MARINE were taking
11:48:24 21 statins, right?

11:48:24 22 A That's correct.

11:48:25 23 Q And none the asserted claims require a statin, right?

11:48:29 24 A They don't require a statin. No.

11:48:31 25 Q And three of them actually say you can't take a statin,

11:48:35 1 right? We talked about that earlier.

11:48:36 2 A Well, I didn't see the word "can't" in there, but I'm not
11:48:39 3 a patent lawyer so --

11:48:41 4 Q I don't think that's disputed; just kidding.

11:48:43 5 Now, REDUCE-IT did not have a monotherapy arm,
11:48:46 6 right, with just Vascepa?

11:48:47 7 A Well, it would have been unethical to have just a Vascepa
11:48:51 8 monotherapy arm. The FDA would never allow it because statin
11:48:56 9 therapy is the standard of care for patients in secondary
11:49:01 10 prevention for high risk diabetic patients.

11:49:03 11 Q Right. And statins like estrogen can affect lipids,
11:49:07 12 right?

11:49:07 13 A Well, of course.

11:49:11 14 MR. KLEIN: All right. Let's go to DDX 10.77.

11:49:11 15 BY MR. KLEIN:

11:49:18 16 Q And you will recognize this as PDX 6.29 from your direct,
11:49:26 17 right?

11:49:26 18 A I do.

11:49:27 19 Q And this is a chart entitled "Omega-3 Fatty Acid
11:49:30 20 Cardiovascular Outcomes Trial Underway As of March 2008,"
11:49:34 21 right?

11:49:34 22 A Yes.

11:49:35 23 Q And so there were eight Omega-3 fatty acids trials in
11:49:40 24 progress as of the alleged conception date, right?

11:49:44 25 A Yes.

11:49:44 1 Q And in fact, all these trials were still pending when
11:49:48 2 Amarin filed its application in 2009, right?
11:49:52 3 A I have to refresh my memory about --
11:49:59 4 Q You can look at the dates. You can look at the dates in
11:50:02 5 the first column.
11:50:02 6 A So you're not asking were they done, just were they
11:50:05 7 initiated?
11:50:06 8 Q Well, they weren't -- let me put this way.
11:50:09 9 None of these study results were published by the
11:50:12 10 time Amarin filed its application in 2009, correct?
11:50:14 11 A I don't believe so.
11:50:15 12 Q Okay. And the fact that there were eight cardiovascular
11:50:20 13 studies, as of March 2008, and as of 2009, showed that there
11:50:25 14 were high expectations that fish oil would have cardiovascular
11:50:29 15 benefits, right?
11:50:30 16 A There were high expectations.
11:50:32 17 Q Yeah. And all eight of these failed.
11:50:34 18 You talk about that, right?
11:50:35 19 A Yes.
11:50:35 20 Q Okay. But a skilled artisan, as of March 2008, would not
11:50:40 21 know that any of these trials were going to fail, right?
11:50:43 22 A As of 2008?
11:50:45 23 Q Right.
11:50:46 24 A That's correct. They were completed after.
11:50:49 25 Q Yeah. And even in 2009, a skilled artisan wouldn't know

11:50:53 1 that any of these studies were going to fail, right?

11:50:55 2 A Correct.

11:50:58 3 Q And none of these trials used pure EPA?

11:51:01 4 A None of them used pure EPA.

11:51:03 5 Q And none of these trials were addressing patients with

11:51:05 6 very high triglycerides, right?

11:51:07 7 A That's correct.

11:51:08 8 Q All right. Now, you talked on direct about how your

11:51:17 9 opinion is that REDUCE-IT showed unexpected results, right?

11:51:20 10 A Oh, yes.

11:51:20 11 Q But Amarin is not the first company to show that purified

11:51:24 12 EPA improves cardiovascular outcomes, can we agree on that?

11:51:29 13 A The JELIS trial had a positive primary composite

11:51:34 14 endpoint, yes.

11:51:35 15 MR. KLEIN: Let's go to DDX 10.78.

11:51:35 16 BY MR. KLEIN:

11:51:38 17 Q And do you recognize DX 1553 as the Yokoyama 2007

11:51:43 18 reference discussing JELIS, right?

11:51:46 19 A I do.

11:51:46 20 Q Okay. And this was published in the Lancet?

11:51:49 21 A Yes.

11:51:49 22 Q Which is a top medical journal, right?

11:51:51 23 A Yes.

11:51:52 24 Q And it had a very strong reputation in the medical

11:51:55 25 community?

11:51:56 1 A Yes.

11:51:56 2 Q In fact, you were a peer reviewer, right?

11:51:59 3 A I'm still a peer reviewer. Yes.

11:52:00 4 Q Okay. You still are?

11:52:01 5 A Yeah.

11:52:02 6 Q Okay. And the peer review process is rigorous at the

11:52:06 7 Lancet, right?

11:52:07 8 A Yes, it is.

11:52:08 9 MR. KLEIN: Okay. Let's go to DDX 0.79.

11:52:11 10 We're still on DX 1553, page 1.

11:52:11 11 BY MR. KLEIN:

11:52:16 12 Q I don't think this is disputed either, but the study was

11:52:19 13 very large. It involved more than 18,000 Japanese patients

11:52:23 14 with a five-year follow-up, right?

11:52:25 15 A Yes.

11:52:27 16 MR. KLEIN: Okay. And let's go to DDX 10.80.

11:52:32 17 This is DX 1553, at page 2.

11:52:32 18 BY MR. KLEIN:

11:52:36 19 Q And Yokoyama used more than 98 percent pure EPA from

11:52:46 20 Mochida, correct?

11:52:48 21 A Yes.

11:52:48 22 Q And Mochida, you understand, makes EpaDEL?

11:52:50 23 A Yes.

11:52:51 24 MR. KLEIN: Okay. Let's go to DDX 10.81.

11:52:51 25

11:52:51 1 BY MR. KLEIN:

11:52:57 2 Q The authors of the Yokoyama reference reported in the
11:53:02 3 *Lancet* that major coronary events were reduced by 19 percent,
11:53:07 4 right?

11:53:07 5 A Yes.

11:53:08 6 Q That's not disputed, correct?

11:53:09 7 A No.

11:53:10 8 MR. KLEIN: Okay. And let's go to DDX 10.82.

11:53:10 9 BY MR. KLEIN:

11:53:12 10 Q And this is the interpretation of the data, in the
11:53:15 11 summary, where the author said,

11:53:19 12 "EPA is a promising treatment for prevention
11:53:22 13 of major coronary events, and especially nonfatal
11:53:26 14 coronary events, in Japanese hypercholesterolemic
11:53:31 15 patients," correct.

11:53:33 16 A Yes.

11:53:33 17 Q Okay. And that conclusion was peer reviewed as well,
11:53:37 18 right?

11:53:37 19 A Yes.

11:53:37 20 Q And this is a pretty simple, straightforward conclusion,
11:53:42 21 right?

11:53:42 22 A It is. There were caveats in the paper, but that is a
11:53:46 23 simple conclusion.

11:53:47 24 Q Okay. And so in view of the JELIS study, a skilled
11:53:51 25 artisan, in March 2008, would have reasonably expected

11:53:54 1 purified EPA to be a promising treatment to prevent major
11:54:00 2 coronary events, correct?

11:54:02 3 A Unstable angina? Yeah.

11:54:05 4 Q Okay. And JELIS did not study DHA, right?

11:54:08 5 A It did not.

11:54:09 6 Q So JELIS provides at least one reason for a skilled
11:54:13 7 artisan, in March 2008, to focus on pure EPA instead of pure
11:54:18 8 DHA, correct?

11:54:19 9 A It -- the JELIS trial did demonstrate some efficacy, but
11:54:28 10 it wasn't in -- here's the problem. And I know that I have
11:54:34 11 stated that JELIS was a nice trial, but in the United States
11:54:39 12 the interpretation would have been as follows.

11:54:41 13 The use of statins in this trial was so low, 5
11:54:49 14 milligrams of Simvastatin, 90 percent of the patients received
11:54:52 15 Simvastatin 5, which no one even uses in the United States at
11:54:57 16 that dose.

11:54:58 17 Ten percent were on Pravastatin 10. The patients
11:54:58 18 had a baseline triglyceride 153. Their LDL was through the
11:54:58 19 ceiling at 184.

11:55:08 20 The problem is that it's not convincing that the use
11:55:10 21 of EPA, over and above a full therapeutic dose of a statin,
11:55:15 22 reduced events.

11:55:16 23 Now, I get it, the primary composite endpoint was
11:55:21 24 positive, but, even the FDA agreed that this study was not
11:55:24 25 applicable to the U.S.

11:55:27 1 Q Okay. And we'll talk about that, I promise. But, it
11:55:30 2 wasn't my question. So, please, listen carefully to my
11:55:34 3 question.

11:55:34 4 A I will, counsel.

11:55:35 5 Q Okay. JELIS provides at least one reason for a skilled
11:55:39 6 artisan to focus on using pure EPA over pure DHA, correct?

11:55:44 7 A Yes, that would be a reasonable conclusion.

11:55:46 8 Q Okay. And just in a short response to your last answer,
11:55:53 9 and we'll get into it in more depth --

11:55:55 10 A Okay.

11:55:55 11 Q -- what you're saying is that JELIS may have -- well, let
11:56:00 12 me ask you the question.

11:56:02 13 Do you agree that the JELIS study reported in the
11:56:06 14 *Lancet*, would have motivated a skilled artisan to run a
11:56:10 15 similar type of study in the United States, to confirm that
11:56:15 16 the results seen in JELIS would apply to a Western population?

11:56:19 17 A Yeah, it is an unsettled issue.

11:56:22 18 Q Okay. And by the way, on direct, you talked about a
11:56:25 19 number of DHA studies related to cardiovascular issues, right?

11:56:29 20 A Yes.

11:56:29 21 Q None of those were outcome studies, correct?

11:56:33 22 A No, but they were also studies that would suggest it
11:56:37 23 would not be smart to throw out the DHA.

11:56:40 24 Q Okay. But those studies were based on biomarkers, right?

11:56:44 25 A Correct. Like all of the studies you used as your

11:56:47 1 principal prior art, none of them were outcome studies either.

11:56:51 2 Q JELIS was an outcome study, right?

11:56:53 3 A Yes. But, this was not part of your principal prior art.

11:56:57 4 Q Okay. Now, you -- and obviously, pure EPA was approved

11:57:00 5 by a regulatory body in Japan, right?

11:57:03 6 A Yes. That's correct.

11:57:04 7 Q But on direct, you didn't talk about any approved pure

11:57:08 8 DHA product, correct?

11:57:11 9 A Approved --

11:57:12 10 Q To reduce -- yeah, to reduce triglycerides.

11:57:14 11 A Yes, that's correct. It was just used investigationally.

11:57:21 12 MR. KLEIN: Now, let's go to DDX 10.122.

11:57:21 13 BY MR. KLEIN:

11:57:27 14 Q This is another document you used during your direct, PX

11:57:32 15 959, pages 1 to 2.

11:57:34 16 Do you remember this one?

11:57:35 17 A Oh, yes.

11:57:36 18 Q Okay. And this is an editorial in the *New England*

11:57:41 19 *Journal of Medicine* called "Fishing For the Miracle of EPA,"

11:57:43 20 right?

11:57:44 21 A Yes. It accompanied publication of the REDUCE-IT trial.

11:57:47 22 Q Right. And you cited this article to discuss praise for

11:57:50 23 REDUCE-IT, right?

11:57:51 24 A Yes.

11:57:51 25 Q And you see the authors also discuss JELIS, right?

11:57:53 1 A Yes.

11:57:54 2 Q And they said,

11:57:55 3 "We find it reassuring that the results

11:58:00 4 reported by Bhatt are similar to those of the Japan

11:58:03 5 EPA Lipid Intervention Study, JELIS, an open label

11:58:08 6 trial, that reported that the risk of major adverse

11:58:10 7 cardiovascular events was 19 percent lower," right?

11:58:13 8 A Yes.

11:58:13 9 Q And they're citing Yokoyama?

11:58:15 10 A They are.

11:58:16 11 Q Yeah. So the authors are not only praising REDUCE-IT,

11:58:19 12 they're also praising all the effort that went into the JELIS

11:58:23 13 study, right?

11:58:23 14 A They are citing it here.

11:58:26 15 Q And they're citing it in support, right?

11:58:30 16 They are citing JELIS to -- for the proposition that

11:58:36 17 they are happy to see that REDUCE-IT confirmed the results of

11:58:39 18 JELIS in a Western population, right?

11:58:42 19 A Well, they didn't say "confirm." They said are "similar

11:58:43 20 to" those of JELIS. Yes.

11:58:45 21 Q Okay. "Similar to," right?

11:58:48 22 So to the authors of the *New England Journal of*

11:58:54 23 *Medicine* editorial are reporting that the results of REDUCE-IT

11:58:57 24 are similar to the results seen in JELIS, correct?

11:58:59 25 A That's what they state.

11:59:01 1 Q Okay. And you understand that Amarin's own documents
11:59:04 2 repeatedly say that JELIS showed that pure EPA reduces
11:59:12 3 cardiovascular risk?

11:59:12 4 A I don't know which documents you're talking about,
11:59:15 5 counsel. I don't know.

11:59:16 6 MR. KLEIN: Okay. Let's go -- and I understand
11:59:17 7 you weren't here for Dr. Ketchum, but let's go to DDX 10.83.
11:59:22 8 And this is DX 1829, page 10.

11:59:22 9 BY MR. KLEIN:

11:59:30 10 Q And here, this is an Amarin internal document, can you
11:59:33 11 see that. There's an Appendix 3. EPA and the JELIS study.

11:59:38 12 And Amarin said in this document, that,
11:59:40 13 "JELIS was set up to test the hypothesis that
11:59:44 14 long-term use of EPA is effective in reduction of
11:59:47 15 major coronary events in Japanese
11:59:51 16 hypercholesterolemia patients given statins," right?

11:59:55 17 A Yes.

11:59:55 18 MR. KLEIN: Okay. Let's go to DDX 10.84, and
12:00:00 19 we're in the same document, DX 1829, page 10.

12:00:00 20 BY MR. KLEIN:

12:00:04 21 Q And in this document they say,
12:00:05 22 "In summary, the JELIS study showed that the
12:00:08 23 frequency of major coronary events is reduced with
12:00:12 24 EPA 19 percent compared to controls."

12:00:15 25 Do you see that?

12:00:16 1 A I do.

12:00:16 2 Q And that's accurately characterizing the JELIS study
12:00:20 3 results, right?

12:00:20 4 A Yes. Based on the primary composite endpoint, yes.

12:00:24 5 MR. KLEIN: Okay. Let's go to DDX 10.85. This
12:00:27 6 is another document we looked at earlier, DX 1862, page 54.

12:00:27 7 BY MR. KLEIN:

12:00:33 8 Q This is the August 2009 presentation that Amarin prepared
12:00:37 9 for a partner, Arisaph. Do you remember talking about that?
12:00:44 10 We talked about that earlier.

12:00:45 11 A Yes, I do.

12:00:46 12 Q Okay. And on this slide, this slide is called "Proven
12:00:50 13 Cardiovascular Outcomes, JELIS Study."

12:00:52 14 Do you see that?

12:00:52 15 A I do.

12:00:53 16 Q And Amarin's description of the JELIS study in this
12:00:58 17 document, for one of its potential partners, is an accurate
12:01:03 18 characterization of the JELIS study results, correct?

12:01:07 19 A "More than 18,000 Japanese patients; all
12:01:10 20 administered statins, primary and secondary
12:01:13 21 prevention; five-year follow-up; 1.8 grams of EPA per
12:01:17 22 day or nothing." Yes.

12:01:19 23 Q Okay. Including the title, "Proven Cardiovascular
12:01:22 24 Outcomes," that accurately characterizes the JELIS study
12:01:26 25 results, right?

12:01:26 1 A For the primary composite endpoint nonstable angina, yes.

12:01:33 2 Q And you didn't see any limitation in this slide to the

12:01:36 3 primary composite endpoint, right?

12:01:38 4 A That's correct, counsel.

12:01:39 5 MR. KLEIN: Okay. Let's go down to DDX 10.86.

12:01:44 6 Here's another slide, DX 1862, page 55.

12:01:44 7 BY MR. KLEIN:

12:01:48 8 Q And this study, this slide says "JELIS Study, EPA Reduces

12:01:54 9 Coronary Events?"

12:01:56 10 Do you see that?

12:01:56 11 A Yes.

12:01:57 12 Q And underneath it says,

12:01:59 13 "EPA Decreased Risks By 53 Percent in

12:02:03 14 Coronary Events in the Patient Subgroup with both

12:02:06 15 high triglycerides and low HDL cholesterol," correct?

12:02:09 16 A It states that.

12:02:10 17 Q Right. And we'll talk about that later.

12:02:12 18 But Amarin is accurately characterizing the JELIS

12:02:15 19 study in slide 55 -- or in DX 1862, page 55, correct?

12:02:21 20 A It's factually correct.

12:02:24 21 Q And you understand that Amarin made similar statements to

12:02:28 22 it's regulator, the FDA, right?

12:02:31 23 A May I see?

12:02:32 24 MR. KLEIN: Sure. Let's go to DDX 10.87, and

12:02:36 25 this is DX 1836. I just have page 71.

12:02:36 1 BY MR. KLEIN:

12:02:40 2 Q But you are familiar with this document where Amarin
12:02:44 3 submitted a formal dispute resolution request related to
12:02:48 4 ANCHOR study, right?

12:02:49 5 A Yes.

12:02:49 6 Q And I'm not going to go through this document in detail
12:02:53 7 because we've done that with another witness, but Amarin told
12:02:56 8 the FDA that it believes that the JELIS study results should
12:03:00 9 not be dismissed lightly, right?

12:03:02 10 A It says that here.

12:03:04 11 Q Okay. But you're not testifying that Amarin overstated
12:03:07 12 the results of the JELIS study to the FDA, right?

12:03:11 13 A No, I'm just offering my own opinion.

12:03:14 14 MR. KLEIN: Okay. Let's go to DDX 10.88. This
12:03:20 15 is a -- this is DX 2235 at page 70.

12:03:20 16 BY MR. KLEIN:

12:03:26 17 Q And can you see that this is a presentation from Amarin
12:03:30 18 to the FDA advisory committee for Vascepa?

12:03:34 19 A Yes.

12:03:35 20 Q Do you see that?

12:03:36 21 A This I haven't seen before.

12:03:38 22 Q Okay. Well, this is the more recent document. You see
12:03:39 23 it's called "Mineral Oil Placebo Analyses"?

12:03:43 24 A Yes.

12:03:43 25 Q And the last bullet says,

12:03:45 1 "A prior trial reported a cardiovascular
12:03:47 2 benefit with EPA consistent with REDUCE-IT," right?
12:03:50 3 A It states that.
12:03:51 4 Q And you can see that Amarin is referring to JELIS as the
12:03:54 5 prior trial that reported a cardiovascular benefit with EPA
12:03:58 6 consistent with REDUCE-IT, right?
12:04:00 7 A It suggests that, yes.
12:04:02 8 Q Okay. And that's an accurate statement that Amarin made
12:04:05 9 to the FDA, right?
12:04:07 10 A I wouldn't dispute what Amarin said.
12:04:11 11 MR. KLEIN: Okay. Let's go to DDX 10.89, and
12:04:17 12 this is PX 583.
12:04:17 13 BY MR. KLEIN:
12:04:20 14 Q This is a 2017 Vascepa operating plan. It's quantitative
12:04:27 15 research by a company called GFK from 2017. Do you see that?
12:04:33 16 A I do.
12:04:33 17 Q Okay. And I'll represent to you -- have you seen this
12:04:37 18 document before?
12:04:37 19 A No, sir.
12:04:38 20 Q Okay. I'll represent to you that it was produced to us
12:04:40 21 from Amarin. Okay?
12:04:42 22 MR. KLEIN: Your Honor, I move into evidence PX
12:04:44 23 583.
12:04:45 24 THE COURT: Any objection?
12:04:46 25 MR. ELIKAN: No objection.

12:04:47 1 MR. KLEIN: Okay.

12:04:48 2 THE COURT: 583 is admitted.

12:04:48 3 (Plaintiffs' Exhibit 583 received in
12:04:50 evidence.)

12:04:50 4 BY MR. KLEIN:

12:04:51 5 Q And so the document is called Vascepa SFE, sales force
12:04:57 6 effectiveness, Q3 2017, Quantitative Research. Do you see
12:05:02 7 that?

12:05:02 8 A Yes.

12:05:03 9 Q And do you understand that Amarin was presenting JELIS
12:05:07 10 data to physicians when marketing Vascepa?

12:05:09 11 A Yes.

12:05:10 12 MR. KLEIN: Okay. Let's go to DDX 10.90. And
12:05:17 13 you can see -- this is PX 583 at page 6.

12:05:17 14 BY MR. KLEIN:

12:05:20 15 Q You can see according to this, this document, the
12:05:25 16 recommendation is to continue to leverage the JELIS data as
12:05:30 17 reduction in cardiovascular events with EPA to explain it is a
12:05:37 18 compelling part of the Vascepa story. Do you see that?

12:05:39 19 A I do.

12:05:40 20 Q And do you understand that Amarin was telling doctors
12:05:43 21 that JELIS data showed a reduction in cardiovascular events?

12:05:46 22 A Yes.

12:05:47 23 Q Okay. And Amarin was not mischaracterizing JELIS to
12:05:51 24 physicians, right?

12:05:52 25 A No, I don't imagine they would.

12:05:54 1 Q Okay. Now -- and, Doctor, you personally have praised
12:05:59 2 the JELIS trial as demonstrating that the addition of EPA to
12:06:03 3 ongoing statin therapy incurred benefit, right?

12:06:06 4 A Say that again, counsel?

12:06:08 5 Q You personally praised the JELIS trial, right?

12:06:11 6 A I have.

12:06:11 7 MR. KLEIN: Let's go to DDX 10.91. This is DX
12:06:18 8 3009. I don't believe this is on the exhibit list so I'll
12:06:22 9 flag that upfront, but I will -- it's being used for
12:06:26 10 impeachment.

12:06:26 11 BY MR. KLEIN:

12:06:28 12 Q This is an article you wrote in 2018 called "Elevated
12:06:32 13 Triglycerides: Diabetes May Be Predictors of Major
12:06:36 14 Cardiovascular Events," right?

12:06:38 15 A Counsel, I didn't write it. It was an article about some
12:06:41 16 research I did.

12:06:42 17 Q I'm sorry, I stand corrected. You were discussed in this
12:06:45 18 article, right?

12:06:46 19 A Yes.

12:06:46 20 Q Okay. You're right.

12:06:48 21 And it says that you and colleagues conducted a
12:06:51 22 retrospective administrative claims analysis of the Optum
12:06:56 23 research database to identify outcomes of patients treated
12:07:00 24 with a statin drug, right?

12:07:02 25 A Yes.

12:07:02 1 Q And the purpose of this study was to further understand
12:07:06 2 the real-world burdens of elevated triglyceride level and
12:07:10 3 diabetes, right?

12:07:11 4 A Yes.

12:07:11 5 Q And if I didn't say this, it was published June 23rd,
12:07:16 6 2018, right?

12:07:16 7 A Well, yeah. But I'll be honest with you, I don't know
12:07:19 8 what the contents of this is, so you'll have to take me
12:07:23 9 through it.

12:07:24 10 MR. KLEIN: Okay. Well, let's go to DDX 10.92.
12:07:28 11 This is a statement attributed to you in the article.

12:07:31 12 THE WITNESS: Okay.

12:07:32 13 MR. KLEIN: Like you said, you didn't write the
12:07:34 14 article.

12:07:35 15 THE WITNESS: Okay.

12:07:35 16 BY MR. KLEIN:

12:07:36 17 Q I want to skip the first sentence, but the next sentence
12:07:39 18 starts,

12:07:40 19 "If the patient's primary residual issue was
12:07:42 20 elevated triglyceride, there is support from the
12:07:45 21 JELIS trial which demonstrated that the addition of
12:07:49 22 EPA to ongoing statin therapy, particularly in
12:07:53 23 patients with triglycerides over 150, incurred
12:07:56 24 benefit."

12:07:57 25 Do you see that?

12:07:57 1 A Yes.

12:07:57 2 Q Is that a statement that you made?

12:08:00 3 A I'm sure it is.

12:08:00 4 Q Okay. And so -- and this is as recent as 2018, right?

12:08:04 5 A Yes.

12:08:04 6 Q Okay. And what -- again, what you said here just to

12:08:09 7 emphasize, is that you characterized the JELIS trial as

12:08:13 8 demonstrating that the addition of EPA to statin therapy

12:08:17 9 incurred cardiovascular benefit, right?

12:08:19 10 A Yes.

12:08:20 11 MR. KLEIN: Okay. Now, let's go to DDX -- oh, I

12:08:22 12 want to move into evidence DX 3009.

12:08:30 13 MR. ELIKAN: Your Honor, it's just been used as

12:08:32 14 impeachment, it's not on the exhibit list. We don't believe

12:08:36 15 it's properly admitted into evidence.

12:08:38 16 He hasn't written it, he's never seen the

12:08:41 17 contents. Principally it's not on the exhibit list which was

12:08:44 18 supposed to be final in January.

12:08:46 19 So, while it's being used as impeachment, that's

12:08:50 20 fine, but we don't understand why it should be admitted.

12:08:53 21 THE COURT: Mr. Klein?

12:08:54 22 MR. KLEIN: The local rule doesn't -- the local

12:08:58 23 rule and the pretrial order just say that impeachment evidence

12:09:01 24 does not have to be on the exhibit list. It doesn't say it

12:09:04 25 can't be introduced during the cross-examination, and Dr. Toth

12:09:08 1 adopted this statement. It's attributed to him in the
12:09:11 2 article.

12:09:13 3 THE COURT: Any response, counsel?

12:09:18 4 MR. ELIKAN: I don't understand how that makes
12:09:20 5 the article admissible. There's a statement, it's attributed
12:09:24 6 to him, all of that is in the record. And the local rules
12:09:28 7 don't say that things that are used for impeachment can be
12:09:31 8 added to the exhibit list.

12:09:33 9 THE COURT: I'm sorry, so is the objection that
12:09:35 10 this is not a document that's been marked as an exhibit or
12:09:40 11 does the objection go to relevance?

12:09:42 12 MR. ELIKAN: It's hearsay, and it's also not on
12:09:44 13 the exhibit list. This is pure hearsay. It's being offered,
12:09:48 14 I think, to prove the truth of the matter asserted. If not,
12:09:51 15 then it's impeachment, and it's being used as such.

12:09:54 16 THE COURT: The objection is overruled.

12:09:55 17 To the extent that the objection is that it's
12:09:57 18 not on the exhibit list, I agree with Mr. Klein, the local
12:10:01 19 rules allow for an exception of impeachment evidence. You
12:10:04 20 don't have to share impeachment evidence in advance of
12:10:07 21 impeaching the witness.

12:10:08 22 As to relevance, Dr. Toth has adopted the
12:10:11 23 statement, and so that would overcome any hearsay objection.

12:10:14 24 The objection is overruled and Exhibit DX 3009
12:10:18 25 will be admitted.

12:10:18 1 (Defendants' Exhibit 3009 received in
12:10:18 evidence.)
12:10:20 2 MR. KLEIN: Thank you. Let's go to another
12:10:22 3 exhibit, DDX 10.112.

12:10:22 4 BY MR. KLEIN:

12:10:28 5 Q Now, Dr. Toth, this is one of your articles, right?
12:10:31 6 A Yes. "Drug Treatment of Hypertriglyceridemia." Yep.
12:10:36 7 Q This is DX 3020, page 12. This is another document being
12:10:40 8 used for impeachment that is not on the exhibit list.
12:10:43 9 This was published in *Drugs* 2010, right?
12:10:48 10 A Yes, that's the date.
12:10:49 11 MR. KLEIN: Okay. And, well, why don't I go
12:10:54 12 ahead and move DX 3020 into evidence.
12:10:59 13 MR. ELIKAN: Your Honor, I object on the same
12:11:01 14 bases as before.
12:11:02 15 THE COURT: Mr. Klein, you need to establish the
12:11:04 16 relevance.
12:11:05 17 MR. KLEIN: Okay.
12:11:05 18 BY MR. KLEIN:
12:11:07 19 Q Section 3.6 of your chart is called Fish Oils, right?
12:11:12 20 A Yes.
12:11:12 21 Q And you say,
12:11:14 22 "The cardiovascular benefits of omega-3 fatty
12:11:18 23 acids, fish oils, EPA, and DHA are well documented,"
12:11:22 24 right?
12:11:22 25 A Yes.

12:11:24 1 MR. KLEIN: And let's go to DDX 10.113.

12:11:24 2 BY MR. KLEIN:

12:11:30 3 Q This is the conclusions of your article, right?

12:11:33 4 A Yes.

12:11:34 5 Q And here I'm just going to read what's highlighted on the

12:11:38 6 screen, and just for the record, it's DX 3020 at page 13.

12:11:42 7 You said,

12:11:43 8 "There is strong evidence to support the use

12:11:45 9 of statins, fibrates, niacin, BAS, and fish oils.

12:11:50 10 Each of these drugs exerts its effects through

12:11:53 11 distinct but often complementary mechanisms."

12:11:58 12 Then you say, "The combination of statins

12:12:00 13 with niacin and fish oils has been studied

12:12:03 14 prospectively in the Haas and JELIS trials

12:12:07 15 respectfully. These combinations are effective and

12:12:12 16 provide incremental benefit beyond statin

12:12:15 17 monotherapy."

12:12:16 18 Is that what you said in the article?

12:12:17 19 A Clearly.

12:12:18 20 MR. KLEIN: Okay. Now I move into evidence DX

12:12:20 21 3020.

12:12:26 22 MR. ELIKAN: No objection.

12:12:26 23 THE COURT: Without any objection DX 3020

12:12:29 24 admitted.

25 ///

12:12:29 1 (Defendants' Exhibit 3020 received in
12:12:29 evidence.)
12:12:31 2 MR. KLEIN: Let's go to DDX 10.96, and this is
12:12:35 3 DX 1709, pages 16 through 17.
12:12:35 4 BY MR. KLEIN:
12:12:41 5 Q And do you recognize this document as
12:12:44 6 "Hypertriglyceridemia: Managing Triglycerides to Reduce
12:12:44 7 Cardiovascular Risk"?
12:12:51 8 A Yes, counsel. You and I have been through this before.
12:12:54 9 Q Yes, right, and this one is on the exhibit list.
12:12:55 10 It was released or published in March 2015, right?
12:12:59 11 A Yes.
12:13:00 12 MR. KLEIN: Okay. I'll go ahead and move in DX
12:13:03 13 1709.
12:13:05 14 MR. ELIKAN: No objection.
12:13:05 15 THE COURT: 1709 is admitted.
12:13:05 16 (Defendants' Exhibit 1709 received in
12:13:08 evidence.)
12:13:08 17 BY MR. KLEIN:
12:13:09 18 Q And this article related to an interview that you had
12:13:13 19 with Dr. Bays, right?
12:13:14 20 A Yes.
12:13:14 21 Q And we had talked about Dr. Bays, and you talked about
12:13:17 22 him, right?
12:13:18 23 A Yes.
12:13:18 24 Q He was the primary investigator for MARINE?
12:13:20 25 A Yes.

12:13:21 1 Q And he asked,

12:13:22 2 "Do we have any clinical trial evidence that

12:13:24 3 administering omega-3 fatty acids reduces

12:13:30 4 atherosclerotic cardiovascular events?"

12:13:33 5 And you replied, "We do. We have two

12:13:36 6 important studies and there are two others in

12:13:38 7 process."

12:13:39 8 I'm not going to read your whole answer, but

12:13:41 9 later on you said,

12:13:42 10 "There is also a nice Japanese study called

12:13:45 11 JELIS in which all the participants were on

12:13:48 12 background statin therapy. The study included both

12:13:51 13 primary and secondary prevention patients. Of note,

12:13:56 14 there was a statistically significant important

12:13:58 15 reduction in the primary composite endpoint, and,

12:14:02 16 once again, in the subgroup of patients with high

12:14:05 17 triglyceride, low HDL, there was a whopping

12:14:09 18 53 percent reduction in risk for the primary

12:14:13 19 composite endpoint."

12:14:14 20 Is that the answer you gave to Dr. Bays'

12:14:16 21 question?

12:14:16 22 A That's the answer I gave.

12:14:19 23 Q And so you told your colleagues back in 2015 and at other

12:14:25 24 points in time that the JELIS cardiovascular results showed

12:14:28 25 promise at a very minimum, right?

12:14:30 1 A Yes, I did. And I take responsibility for that.

12:14:34 2 But I also take responsibility for the fact that I

12:14:38 3 didn't do a great job of looking under the hood of the entire

12:14:43 4 spectrum of results in the study, and, instead, I just focused

12:14:48 5 on the primary composite endpoints.

12:14:50 6 And when I say "looking under the hood," I didn't do

12:14:53 7 a very critical analysis of all the endpoints that were

12:14:56 8 offered in the study which showed considerable weaknesses in

12:14:59 9 the study.

12:15:00 10 But that quote is mine.

12:15:02 11 Q Okay. When you referred to "looking under the hood,"

12:15:04 12 what you're talking about is the efforts that you undertook as

12:15:08 13 an expert witness retained by Amarin for this case, right?

12:15:12 14 A Well, actually, it stemmed from a lot of issues.

12:15:19 15 When the REDUCE-IT trial first came out, there were

12:15:24 16 lots of questions swirling about how well do the studies stack

12:15:29 17 up together, and when you did look under the hood and read the

12:15:31 18 FDA report, there were lots of issues concerning the

12:15:35 19 individual endpoints, and we've revealed that in testimony

12:15:38 20 yesterday and today.

12:15:40 21 Q And the issues you're talking about are issues relating

12:15:43 22 to whether the JELIS trial study design would meet the FDA

12:15:47 23 requirements for a clinical study to support a new indication,

12:15:53 24 right?

12:15:53 25 A And the large number of differences between the outcomes

12:15:56 1 of the studies and how significant different outcomes were
12:16:01 2 between the two. So, yeah, there are a lot of differences
12:16:04 3 between them.

12:16:04 4 Q Okay. And you understand when the FDA addressed Amarin's
12:16:09 5 characterizations of the JELIS trial, that was in the context
12:16:13 6 of Amarin requesting a new FDA-approved indication, right?

12:16:17 7 A I would imagine. But JELIS also did not get Epadel any
12:16:24 8 approval in the United States, and the reason for that is
12:16:27 9 there were weaknesses in the study.

12:16:28 10 Q And you certainly understand that to get approval of a
12:16:33 11 drug by the FDA in the United States is a very rigorous
12:16:37 12 process, right?

12:16:38 13 A Yes, it is.

12:16:41 14 MR. KLEIN: Now, let's go to DDX 10.97.

12:16:41 15 BY MR. KLEIN:

12:16:49 16 Q And remember you talked in the interview with Dr. Bays
12:16:52 17 about a whopping 53 percent increase?

12:16:55 18 A Yes, I did.

12:16:55 19 Q Okay. You were referring to this Saito article, I
12:16:59 20 believe?

12:16:59 21 A Yes.

12:17:00 22 Q From 2008?

12:17:01 23 A I was.

12:17:03 24 MR. KLEIN: And Saito is DX 1547, and I'm
12:17:05 25 referring to pages 1 and 5. This is on the exhibit list so I

12:17:08 1 would move it into evidence.

12:17:10 2 MR. ELIKAN: No objection.

12:17:11 3 THE COURT: 1547 is admitted.

12:17:11 4 (Defendants' Exhibit 1547 received in
12:17:14 5 evidence.)

12:17:14 5 BY MR. KLEIN:

12:17:14 6 Q Okay. And I'm just going to summarize the results at the
12:17:17 7 bottom of the snapshot on the screen.

12:17:20 8 Saito reported that,

12:17:21 9 "Those with abnormal levels, triglycerides
12:17:24 10 above 500, and HDL under 40 milligrams per deciliter
12:17:30 11 had significantly higher CAD hazard ratio. In this
12:17:37 12 higher risk group EPA treatment suppressed the risk
12:17:40 13 of CAD by 53 percent," right?

12:17:44 14 A Yes, when you look at the Yokoyama parent manuscript, it
12:17:48 15 said that the study was not powered to perform subgroup
12:17:51 16 analyses, and so this particular analysis would have to be
12:17:56 17 regarded as hypothesis generating only.

12:17:59 18 Q But this hypothesis was published, correct?

12:18:02 19 A Yeah, sure, it was.

12:18:03 20 Q And a skilled artisan at least as of June 2008 would have
12:18:07 21 seen Saito, right?

12:18:09 22 A They could have, yes.

12:18:11 23 Q And, now, I want to talk about that date because
12:18:15 24 June 2008 is after March 25th, 2008, right?

12:18:19 25 A Yes.

12:18:20 1 MR. KLEIN: Okay. Let's go to DDX 10.98, and
12:18:26 2 that is DX 1524 pages 39, and 13 and 14.

12:18:26 3 BY MR. KLEIN:

12:18:34 4 Q And this is the WO '118 reference. Do you remember this?

12:18:39 5 A Yes.

12:18:41 6 Q And it's dated December 13th, 2007, right?

12:18:46 7 A Do you remember this?

12:18:49 8 Can I see another part of the document just to
12:18:52 9 refresh my memory?

12:18:53 10 Q Sure, you should have DX 1524 in your binder, I hope.

12:18:57 11 A 1524. I do.

12:19:14 12 Okay. Go ahead, counsel.

12:19:23 13 Q All right. This reference from 2007 talks about -- well,
12:19:30 14 you see the bottom Figure 2, you see Figure 2 is a graph
12:19:34 15 prepared by plotting the incidence of cardiovascular event for
12:19:37 16 patients having risk factors of triglycerides of at least
12:19:41 17 150 milligrams per deciliter?

12:19:43 18 A Yes.

12:19:43 19 Q Okay. If we go DDX 10.99, this is DX 1524, page 2, this
12:19:55 20 is a figure that's representing what the Saito reference was
12:20:00 21 talking about, right?

12:20:01 22 A Yes.

12:20:01 23 Q Okay. And then if we go to DDX 10.100, this reference
12:20:09 24 says,

12:20:10 25 "As evident from Table 3 and Figure 2, EPA

12:20:16 1 significantly suppressed occurrence of cardiovascular
12:20:19 2 events in the patients having the risk factors of
12:20:21 3 triglycerides of at least 150, and the rate of
12:20:25 4 suppression of the cardiovascular event occurrence
12:20:28 5 was 53 percent," referring back to Figure 2, right?
12:20:32 6 A Yes.
12:20:32 7 Q So, in short, this reference from 2007 is revealing to a
12:20:36 8 skilled artisan the same information that the Saito 2008
12:20:39 9 reference talked about?
12:20:40 10 A Yes. But, it was hypothesis generating only.
12:20:44 11 Q Okay. And this, just to be clear, was before March 25th,
12:20:48 12 2008, right?
12:20:48 13 A Yes.
12:20:49 14 Q Now, Doctor, in view of all the documents we reviewed
12:20:56 15 from the prior art and Amarin and your own articles, JELIS
12:21:00 16 clearly provided at least a reasonable expectation of
12:21:03 17 achieving the same type of cardiovascular events and outcomes
12:21:08 18 that we saw in REDUCE-IT, right?
12:21:10 19 A With big differences between the studies.
12:21:13 20 Q Yeah, but JELIS would have provided a reasonable
12:21:15 21 expectation that what we saw in REDUCE-IT, we would get
12:21:20 22 something similar, right?
12:21:21 23 A Perhaps.
12:21:23 24 Q Okay.
12:21:24 25 A My beef with it is that the statins were profoundly

12:21:28 1 underdosed, and you don't know if would you have reproduced
12:21:32 2 that data with more appropriate Western level statin dosing,
12:21:36 3 and that's a big problem.

12:21:37 4 Q Okay. And, in your view, what REDUCE-IT did was prove
12:21:43 5 that the JELIS study results can translate to a western
12:21:47 6 population correct?

12:21:49 7 A No, I wouldn't say that.

12:21:49 8 Q JELIS didn't prove that?

12:21:51 9 A That -- that it proves what JELIS -- say it again.

12:21:55 10 Q Okay. JELIS proved -- sorry.

12:22:00 11 REDUCE-IT proved that pure EPA can be used and
12:22:07 12 achieve coronary benefits similar to those that were achieved
12:22:12 13 in Japanese patients in the JELIS study, correct?

12:22:14 14 A The REDUCE-IT trial went far beyond that, but it did show
12:22:19 15 that the use of EPA in combination with a statin does provide
12:22:23 16 across-the-board, incremental reductions in cardiovascular
12:22:26 17 events, yes.

12:22:28 18 MR. KLEIN: Okay. Now, let's go back to DDX
12:22:31 19 10.101 where we started.

12:22:31 20 BY MR. KLEIN:

12:22:34 21 Q Okay. Now, despite everything we've discussed so far, do
12:22:38 22 you still dispute the simple logic of defendants' obviousness
12:22:43 23 theory?

12:22:46 24 A Yes, I do.

12:22:47 25 Q Okay. Now, Doctor, you've got a long -- you've had

12:22:51 1 longstanding business relationships with Amarin, right?

12:22:54 2 A Yes, counsel. Here we go.

12:22:56 3 Q Yep. Okay.

12:22:58 4 You've been a member of Amarin's Speakers Bureau for

12:23:01 5 five, six years, something like that?

12:23:04 6 A Lay it on me, man.

12:23:05 7 Q You have to say yes or no.

12:23:06 8 A Yes. Yes, counsel.

12:23:07 9 Q And you lecture to other physicians and healthcare

12:23:11 10 providers about Vascepa?

12:23:12 11 A I do; very proudly, too.

12:23:14 12 Q Okay. And you're still a member of Amarin's Speakers

12:23:18 13 Bureau, right?

12:23:18 14 A Yes.

12:23:19 15 Q You've consulted with Amarin on a variety of research

12:23:22 16 projects?

12:23:23 17 A Yes, important projects.

12:23:25 18 Q Over the years you've entered into a number of consulting

12:23:28 19 agreements was Amarin, right?

12:23:30 20 A Probably -- well, one that led to 14 publications.

12:23:35 21 That's the major one. I don't know if there's another

12:23:38 22 consulting arrangement. I am a member of the Speakers Bureau,

12:23:42 23 uh-huh.

12:23:43 24 Q Well, you were a consultant to Amarin in connection with

12:23:49 25 the REDUCE-IT study, right?

12:23:50 1 A No, I was not an investigator in REDUCE-IT.

12:23:52 2 Q Uh --

12:23:54 3 A I was an investigator in STRENGTH, but not REDUCE-IT.

12:23:59 4 Q So you did not have a consultancy relationship with

12:24:02 5 Amarin concerning the REDUCE-IT study?

12:24:04 6 A No, sir, not apart from this case.

12:24:07 7 Q All right. But you've repeatedly worked with Amarin to

12:24:11 8 publish articles, right?

12:24:12 9 A Yeah, yeah.

12:24:13 10 Q And you know the scientists at Amarin?

12:24:15 11 A You know, I don't know scientists at Amarin. We've done

12:24:19 12 strictly clinical database research, and I have not had

12:24:24 13 contact with Amarin scientists per se.

12:24:27 14 Q What about Seffy Philip and Craig Granowitz?

12:24:31 15 A Yeah, they're not Amarin scientists, they're -- Craig is

12:24:35 16 the medical director and Seffy Philip is a pharmacologist, but

12:24:40 17 he doesn't do research.

12:24:41 18 Q I see, okay. I'm sorry to use the term scientist. But

12:24:45 19 you certainly know those individuals at Amarin, right?

12:24:47 20 A Yes, I do.

12:24:48 21 MR. KLEIN: Okay. Let's go to DDX 10.114.

12:24:48 22 BY MR. KLEIN:

12:24:56 23 Q And I'm going to go through these slides quickly. I'm

12:24:59 24 not going to discuss the substance or even move them into

12:25:02 25 evidence.

12:25:03 1 But generally there are three references on DDX
12:25:11 2 10.114 where you were co-authoring articles in the last two
12:25:16 3 years with individuals from Amarin, right?
12:25:18 4 A Yes.
12:25:18 5 Q Okay. And some of these articles even disclose that
12:25:24 6 you're a consultant or speaker for Amarin, right?
12:25:26 7 A Oh, they all do.
12:25:28 8 MR. KLEIN: And, for the record, I don't think I
12:25:29 9 need to move them in, it's DX 3010, DX 3011 and DX 3012.
12:25:35 10 And could we go to DDX 10.115.
12:25:35 11 BY MR. KLEIN:
12:25:39 12 Q This demonstrative shows three more articles along the
12:25:43 13 same lines, right?
12:25:43 14 A Oh, there will be more.
12:25:45 15 Q Yeah, that was my next question. Okay.
12:25:48 16 And Amarin has paid you substantial sums for
12:25:55 17 consulting work unrelated to this case, right?
12:25:58 18 A I wouldn't call it substantial sums, but they've paid me.
12:26:02 19 MR. KLEIN: Okay. Let's go to DDX 10.108.
12:26:02 20 BY MR. KLEIN:
12:26:08 21 Q Doctor, you're aware that payments to you from Pharma
12:26:12 22 companies, not just you but all doctors, are publicly
12:26:16 23 available on a government website?
12:26:17 24 A Yes, it's a favorite site for newspaper reporters and
12:26:22 25 lawyers.

12:26:22 1 Q I know what you're referring to. I'm not getting into
12:26:26 2 those newspaper articles so you'll be relieved.

12:26:29 3 All right. On the screen is DX 3017 which is not in
12:26:33 4 evidence and was not on the exhibit list, although we've
12:26:36 5 disclosed it to counsel.

12:26:38 6 I will represent to you that this comes from cms.gov
12:26:43 7 which is the government website that hosts the database on
12:26:47 8 payments to doctors. You're familiar with that, right?

12:26:49 9 A Yeah, it's part of the Sunshine Act.

12:26:51 10 Q CMS is a Center for Medicare and Medicaid Services,
12:26:55 11 right?

12:26:55 12 A Yes.

12:26:55 13 Q And the page or on the screen discusses the process for
12:26:59 14 submitting payments to the open payment database. Are
12:27:01 15 generally familiar with that process?

12:27:04 16 A I'm not because I pay no attention to it.

12:27:07 17 Q Okay. But generally, according to the website, the way
12:27:10 18 it works is that companies like Amarin submit data to the
12:27:16 19 government. You understand that, right?

12:27:17 20 A I do.

12:27:17 21 Q And then there's a process where the physicians and
12:27:20 22 teaching hospitals can review and dispute the data. Do you
12:27:23 23 understand that?

12:27:23 24 A I do.

12:27:24 25 Q And then the data is displayed on the public -- the CMS

12:27:29 1 **public website, right?**

12:27:30 2 A **Yes, in bright, fluorescent light.**

12:27:33 3 Q **And CMS -- I can't remember if I said this, for the record, that's Center For Medicare and Medicaid Service, right?**

12:27:40 6 A **Yes; known for it's accuracy.**

12:27:43 7 Q **Okay.**

12:27:43 8 A **No, that's not true.**

12:27:45 9 MR. KLEIN: **Let's go to DDX 10.109.**

12:27:45 10 **BY MR. KLEIN:**

12:27:53 11 Q **And just to be clear, you understand that CMS requires organizations like Amarin to keep records for at least five years?**

12:28:01 14 A **I do.**

12:28:01 15 Q **All right. And that there are stiff penalties, up to a million dollars. If the pharma company fails to report information in a timely, accurate, or complete manner?**

12:28:11 18 A **That I didn't know. But they do report timely, yes.**

12:28:15 19 MR. KLEIN: **Okay. Let's go to DDX 10.110.**

12:28:15 20 **BY MR. KLEIN:**

12:28:22 21 Q **Okay. Now, Doctor, I will represent to you that DX 3006 on the screen summarizes data from the documents that are cited, which is DX 3000 through DX 3005, and those are spreadsheets from the CMS website reflecting payments from Amarin to physicians from 2013 to 2018. Okay? I'm**

12:28:49 1 representing that to you.

12:28:50 2 A Sure.

12:28:51 3 Q And I'll also represent to you that when we prepared
12:28:54 4 this, we removed any expenses that you were reimbursed for
12:28:58 5 food, lodging, et cetera.

12:28:59 6 A Okay, counsel.

12:29:00 7 Q Okay. And according to -- I'll also for the record
12:29:03 8 represent that this document has been disclosed to the other
12:29:06 9 side in advance.

12:29:08 10 And so if we look at DX 3006, according to the
12:29:15 11 exhibit, Amarin over the years from 2013 to 2018 has paid you
12:29:20 12 about \$140,000. Do you see that?

12:29:22 13 A That's what the figure says.

12:29:24 14 Q Okay.

12:29:24 15 A But there's a problem.

12:29:25 16 Q Okay. Well, I'm going to ask you the next question. Has
12:29:29 17 Amarin paid you about \$140,000 from 2013 to 2018?

12:29:34 18 A I'm not sure. I haven't tallied it. But I'll tell you
12:29:38 19 right now, based on 1099s for 2016, the accurate number was
12:29:43 20 \$4,875. For 2017, my 1099 was for 10,800.

12:29:49 21 That's a three-fold difference for both of those
12:29:52 22 years, and the CMS database is notoriously inaccurate.

12:29:57 23 So, no, I don't agree, and I don't know how much
12:29:59 24 they paid me, but for those two years the figures are off
12:30:03 25 three fold.

12:30:04 1 Q Okay. Doctor, you knew I was going ask you these
12:30:08 2 questions, right?

12:30:08 3 A Of course I knew you were going to ask me these
12:30:11 4 questions, yes.

12:30:12 5 Q Okay. Did you do any investigation to find out how much
12:30:16 6 Amarin did, in fact, pay you?

12:30:18 7 A I did not.

12:30:18 8 Q Okay. And has Amarin paid you additional funds in 2019?

12:30:23 9 A Yes. In the same way that you have billable hours, they
12:30:26 10 did pay me for being part of this case, yes.

12:30:29 11 Q No, just to be clear, I'm not asking about any payments
12:30:32 12 about this case. Has Amarin made payments to you unrelated to
12:30:36 13 this case in 2019?

12:30:38 14 A Yes, they did.

12:30:40 15 Q About how much?

12:30:41 16 A Again, I haven't received my 1099 yet. But I probably
12:30:46 17 gave five or six talks last year. But, again, I'm not sure.

12:30:51 18 Q Doctor, I understand you're not sure, but is it fair to
12:30:55 19 say that Amarin has paid you about a hundred thousand dollars
12:30:57 20 unrelated to this case?

12:30:59 21 A Again, I'm not sure.

12:31:00 22 Q Okay. Would that surprise you?

12:31:02 23 A Would it surprise me? That would surprise me.

12:31:06 24 Q That would surprise you.

12:31:09 25 Okay. So Amarin, at a minimum, has paid you at

12:31:13 1 least \$70,000. Do you agree with that?

12:31:16 2 A Counsel, I would have to look. And I'm being very honest

12:31:20 3 with you. I have so many things to do, the last thing that I

12:31:23 4 thought of was to come in here and add up what Amarin paid me

12:31:29 5 last year.

12:31:30 6 MR. KLEIN: Okay. Let's play page 334 of his

12:31:33 7 deposition, lines 15 to 23.

12:31:35 8 (Deposition video recording played.)

12:32:10 9 BY MR. KLEIN:

12:32:11 10 Q Was that your testimony?

12:32:11 11 A You just saw it.

12:32:13 12 Q Okay. I have to ask you that question.

12:32:14 13 A Yes, counsel.

12:32:16 14 MR. KLEIN: Okay. I have no further questions

12:32:19 15 at this time, but I would like to move into evidence the CMS

12:32:23 16 documents that we reviewed which were used for impeachment, DX

12:32:26 17 3000 to 3006; and 3017 and 3018.

12:32:39 18 THE COURT: Any objection?

12:32:40 19 MR. ELIKAN: Your Honor, may I have one moment?

12:32:43 20 THE COURT: Yes.

12:32:51 21 (Discussion held off the record.)

12:32:51 22 MR. ELIKAN: We do object, Your Honor.

12:32:52 23 This includes 7,000 pages of spreadsheets that

12:32:56 24 were produced to us on Saturday night. We've been unable to

12:33:00 25 review them, at least not thoroughly. There are 6,000 or

12:33:04 1 7,000 pages.

12:33:05 2 I would love to hand up a tiny bit so you can
12:33:09 3 see what we're talking about. It's not restricted to
12:33:12 4 Dr. Toth, it's an entire spreadsheet produced to us in pdf
12:33:17 5 form. We don't think it's admissible for a variety of
12:33:21 6 reasons.

12:33:22 7 But at the end of the day, it's hearsay, and it
12:33:25 8 doesn't fit under any possible exception to the hearsay rule,
12:33:31 9 and, additionally, it's a set of documents that is notoriously
12:33:38 10 suspect.

12:33:38 11 So, we don't see how this is -- how this should
12:33:42 12 be admitted under any hearsay exception or that the Court -- I
12:33:45 13 think the other argument is that judicial notice should be
12:33:49 14 taken of it.

12:33:50 15 We have a variety of articles from the AMA, from
12:33:54 16 *Endovascular Today*, both pointing out that the CMS website is
12:34:00 17 erroneous and erroneous to very high degree. I think
12:34:08 18 *Endovascular Today* said it was shockingly erroneous with an
12:34:11 19 error rate of, I believe, 30 percent.

12:34:11 20 So we don't see why this document should be
12:34:14 21 coming into evidence. It's clearly hearsay. It's not the
12:34:17 22 statements of Amarin, but instead of CMS. It may be based on
12:34:23 23 materials provided by Amarin but not simply passed through.

12:34:27 24 And there's absolutely no foundation for
12:34:30 25 Dr. Toth to address the entirety of this vast spreadsheet

12:34:36 1 which concerns every doctor to whom Amarin has made any
12:34:40 2 payment.

12:34:42 3 So we don't see that as being any -- we don't
12:34:46 4 see it fitting under any hearsay rule, but, more broadly, it's
12:34:49 5 something that's there's been no foundation laid for it.
12:34:53 6 There's a summary slide, but Dr. Toth has said that the
12:34:56 7 summary slide is erroneous.

12:34:58 8 You need to have -- the bottom line is you need
12:35:01 9 to have the spreadsheets underneath be admissible. They
12:35:05 10 haven't even called a witness to sponsor it.

12:35:07 11 If a witness were called, we'd be asking about
12:35:10 12 the AMA position and the accountings taken of it, taken by
12:35:17 13 *Endovascular Today* and variety of other sources.

12:35:20 14 How Dr. Toth's testimony about the summary sheet
12:35:23 15 not being accurate could somehow lead to admissibility of
12:35:28 16 7,000 pages is -- we just think it's not supported.

12:35:33 17 THE COURT: So let me take this one step at a
12:35:35 18 time.

12:35:39 19 DX 3018 is a cms.gov website, and I haven't
12:35:47 20 looked at the actual document, but am I assuming that there
12:35:50 21 are voluminous -- I'm sorry, do DX 3017 and 3018 both relate
12:36:00 22 to information on cms.gov; is that right?

12:36:05 23 MR. KLEIN: Correct. Those are just website
12:36:07 24 pages, I believe.

12:36:08 25 THE COURT: So they're not -- they just consist

12:36:10 1 of basically two pages.

12:36:12 2 MR. KLEIN: Correct. Yes. I think that's
12:36:13 3 right.

12:36:14 4 THE COURT: So let me take that objection first.
12:36:17 5 With respect to DX 3017 and 3018, why can't I just take
12:36:24 6 judicial notice of the website?

12:36:26 7 MR. ELIKAN: That we don't have any objection
12:36:28 8 to, it's about the spreadsheet and the summary.

12:36:30 9 THE COURT: All right. So that's why I'm taking
12:36:33 10 this one at a time. There's no objection to DX 3017 and 3018.
12:36:39 11 Therefore I'm admitting those two exhibits.

12:36:39 12 (Defendants' Exhibit 3017 and 3018
12:36:45 13 received in evidence.)

12:36:45 13 THE COURT: And then there are two more
12:36:47 14 documents, 3000, and then 3006 is just a summary.

12:36:55 15 MR. KLEIN: I think it's 3000 through 3006. The
12:36:59 16 way this is organized, it's one spreadsheet per year, and each
12:37:05 17 spreadsheet shows Amarin's payments to physicians.

12:37:12 18 THE COURT: It would be 3000 to 3005.

12:37:15 19 MR. KLEIN: Those are the spreadsheets.

12:37:17 20 THE COURT: And 3006 is the summary.

12:37:20 21 MR. KLEIN: Correct.

12:37:20 22 THE COURT: And as I understand the objection --
12:37:25 23 is the main objection, Mr. Elikan, that DX 3000 to 3005
12:37:32 24 contain information about payments to others aside from
12:37:37 25 Dr. Toth?

12:37:39 1 MR. ELIKAN: Yes. And additionally it's
12:37:42 2 **inadmissible hearsay as to Dr. Toth.**
12:37:44 3 There's nobody who has authenticated it. It
12:37:48 4 seems to be clearly inadmissible hearsay. It doesn't fall
12:37:51 5 within the sort of matter that's usually addressed by judicial
12:37:55 6 notice. For example --
12:37:58 7 THE COURT: Hang on. Is there any dispute that
12:38:00 8 they come from the cms.gov website?
12:38:04 9 MR. ELIKAN: I am -- I don't know for sure, but
12:38:06 10 I would accept Mr. Klein's representation that --
12:38:09 11 THE COURT: Why is that not a public record
12:38:12 12 **exception?**
12:38:13 13 MR. ELIKAN: I'm sorry, Your Honor?
12:38:15 14 THE COURT: Why doesn't it fall within the
12:38:17 15 **public records exception?**
12:38:19 16 MR. ELIKAN: So the public records exception, it
12:38:21 17 has to lay out -- set out the offices activities or fit within
12:38:25 18 one of the other requirements.
12:38:27 19 We don't see it fitting into any of the rules in
12:38:30 20 803-8, and it also asked not indicate a lack of
12:38:35 21 **trustworthiness.**
12:38:36 22 We already heard from Dr. Toth that it's
12:38:40 23 **inaccurate, and I have a bevy materials that, if there were a**
12:38:40 24 **witness sponsoring it, we could ask that witness about that**
12:38:46 25 **show a lack of trustworthiness.**

12:38:46 1 THE COURT: Does Amarin have a record of how
12:38:49 2 much it's paid Dr. Toth within the last -- from 2013 and 2018
12:38:53 3 that's different than what's indicated on the CMS.gov website?

12:38:58 4 MR. ELIKAN: As far as whether there's a
12:39:00 5 different record, I don't know. We got these in the middle of
12:39:04 6 trial. We would have to decipher the spreadsheet and figure
12:39:07 7 that out.

12:39:08 8 THE COURT: So here's my issue. I think that
12:39:10 9 it's proper impeachment evidence to show how much a witness
12:39:14 10 has been paid by a party unrelated, whether its an expert fee
12:39:19 11 or other relationship. So I think it's a fair area of
12:39:25 12 inquiry.

12:39:25 13 And if the only information that is available is
12:39:27 14 is what is on a government website, I can take weight of that
12:39:31 15 evidence if I have testimony that information on that website
12:39:36 16 might not be entirely accurate.

12:39:37 17 But if what is shown is what Amarin submitted to
12:39:40 18 the agency, then I certainly can admit that. But, if Amarin
12:39:47 19 is telling me that what's on that -- the website is incorrect,
12:39:52 20 I would want to give Amarin the opportunity to say here's a
12:39:55 21 correct record of what we paid.

12:39:56 22 I think this is all a fair area of inquiry. It
12:39:59 23 shouldn't be any surprise to anyone. Dr. Toth recognized that
12:40:03 24 he would be asked. He was asked in his deposition.

12:40:07 25 So I don't want there to be any gamesmanship, in

12:40:09 1 other words. I don't have to have the exact number of
12:40:13 2 payments, but there was at least testimony that he was paid
12:40:15 3 around 70, \$69,000.

12:40:18 4 MR. KLEIN: Something like that.

12:40:18 5 THE COURT: As of July 2019.

12:40:20 6 MR. ELIKAN: So, Your Honor --

12:40:20 7 THE COURT: So I want you to be able to resolve
12:40:22 8 this issue is my point, otherwise I'll admit it and give it
12:40:26 9 whatever weight it deserves.

12:40:29 10 MR. ELIKAN: Your Honor, just two brief points.

12:40:31 11 We think in any event, if Your Honor was to admit these
12:40:36 12 spreadsheets, they ought to be redacted so they only have

12:40:39 13 Dr. Toth's --

12:40:40 14 THE COURT: Yes, I agree with that, yes.

12:40:40 15 MR. ELIKAN: And we --

12:40:40 16 THE COURT: But that's not your sole objection
12:40:40 17 because that's an easy objection, I already decided that
12:40:40 18 because your objection is that it includes information
12:40:45 19 relating to other individuals. I agree I would redact that.

12:40:49 20 MR. ELIKAN: And as far as the summary chart
12:40:52 21 goes, there hasn't been any--

12:40:53 22 THE COURT: So does that mean you no longer have
12:40:56 23 objection to 3000 to 30005? Let's focus on that first. If I
12:41:00 24 redact the information relating to payments to others?

12:41:04 25 MR. ELIKAN: I'm advised that we're okay with

12:41:06 1 that. If that's --

12:41:09 2 THE COURT: All right.

12:41:09 3 MR. KLEIN: Can I speak that, please?

12:41:12 4 THE COURT: To what issue, payments to others?

12:41:14 5 MR. KLEIN: To redaction, the redaction issue.

12:41:15 6 THE COURT: Uh-huh.

12:41:16 7 MR. KLEIN: We would request -- we're okay with
12:41:19 8 redactions, but we would ask that the information with regard
12:41:21 9 to Dr. Budoff not be redacted, and because, in view of his
12:41:26 10 testimony a couple weeks ago where he testified at deposition
12:41:29 11 that he received \$300,000 personally, and then he testified on
12:41:33 12 the stand that it went to his institution, the database is
12:41:38 13 consistent with his deposition.

12:41:40 14 And I think that maybe the heart of this
12:41:43 15 dispute, and I've been trying to work it out with counsel to
12:41:46 16 try to find out how much these experts have actually been
12:41:50 17 paid, which is the information that I personally would like,
12:41:53 18 but the information as to Dr. Budoff we submit is relevant to
12:41:57 19 his trial testimony.

12:41:59 20 And I'm okay with redacting out everyone else,
12:42:03 21 but I would request that we keep in Dr. Toth and Dr. Budoff
12:42:07 22 for the spreadsheets given that both of these witnesses
12:42:10 23 testified.

12:42:11 24 THE COURT: Is there any objection to that
12:42:13 25 proposal?

12:42:14 1 MR. ELIKAN: Yes. Dr. Budoff is not here to
12:42:16 2 answer questions about any of this information. He's back
12:42:20 3 in -- at his home.

12:42:22 4 And Your Honor mentioned the ability that Your
12:42:24 5 Honor can take it with weight. Without a sponsoring witness,
12:42:27 6 we don't have anyone to cross-examine with these many
12:42:31 7 statements about the inaccuracies, the very high level of
12:42:36 8 inaccuracies in the database.

12:42:38 9 THE COURT: Well, I do have -- Dr. Toth just
12:42:41 10 testified that he thinks the database is not reliable.

12:42:44 11 MR. ELIKAN: You have testimony from Dr. Toth to
12:42:47 12 that effect, but, Your Honor, we can't introduce all these
12:42:50 13 articles about the --

12:42:52 14 THE COURT: Wait. So I thought there was no
12:42:53 15 objection to the data at least with respect to this witness.

12:42:56 16 MR. ELIKAN: Were that to resolve the issue,
12:42:59 17 Your Honor, we --

12:43:00 18 THE COURT: So are you withdrawing your
12:43:02 19 representation that there's no objection?

12:43:06 20 And maybe let's do this. Let's -- to be fair,
12:43:09 21 let's do this. We're kind of at a break point anyways.

12:43:12 22 I'll take a lunch break, I want counsel to work
12:43:15 23 out this issue if you're able to, but, I can tell you my
12:43:20 24 inclination is to admit the spreadsheet with respect to
12:43:25 25 Dr. Toth.

12:43:25 1 But, the summary -- I mean, if the summary is
12:43:29 2 just summarizing all the numbers as added up, I don't see any
12:43:35 3 objection. It will avoid me having to add up the numbers on
12:43:37 4 my own.

12:43:37 5 With respect to Dr. Budoff, I'm a little
12:43:42 6 concerned that this information was not introduced during his
12:43:45 7 examination to allow him the opportunity to say -- to
12:43:49 8 challenge the information.

12:43:50 9 I know that I have his testimony about how much
12:43:53 10 he was paid and he disputes some of the payments whether they
12:43:56 11 went to him or his institution. So with him, I'm inclined not
12:44:00 12 to admit the information because he's not here.

12:44:02 13 | MR. KLEIN: Can I --

12:44:03 14 THE COURT: But you can try to resolve it if you
12:44:05 15 can.

12:44:06 16 MR. KLEIN: Can I just respond to that last
12:44:07 17 point real quickly?

12:44:09 18 Obviously in his deposition he said he was paid
12:44:12 19 personally 300,000. So there was no reason for me to believe
12:44:15 20 that he would contradict that on the stand.

12:44:18 21 THE COURT: But you have his deposition
12:44:20 22 testimony, that's already in.

12:44:20 23 | MR. KLEIN: Right.

12:44:21 24 THE COURT: You used that to impeach him.

12:44:24 25 MR. KLEIN: Right. But as we prepared for

12:44:25 1 Dr. Toth's deposition and went through the spreadsheet, we
12:44:29 2 realized that the information for Dr. Budoff did not say the
12:44:31 3 payments went to his institution, they went to him personally,
12:44:35 4 and that's why we would want that information introduced as
12:44:38 5 well.

12:44:38 6 Now, we did raise this issue with counsel and
12:44:41 7 said if it went to his institution, by all means, let us know,
12:44:45 8 and that's fine, and we'll drop the issue but they did not
12:44:48 9 give us any evidence.

12:44:48 10 THE COURT: But my point is you didn't offer
12:44:51 11 this during Dr. Budoff's testimony.

12:44:53 12 MR. KLEIN: No. That's true. That's true. But
12:44:55 13 I did not focus on whether the payments went to him or his
12:44:59 14 institution because he admitted it went to him personally.

12:45:02 15 THE COURT: All right. That's -- I gave you my
12:45:04 16 preliminary thoughts. You can try to see if you can resolve
12:45:08 17 it. If not, I'll give you my ruling after lunch.

12:45:12 18 MR. KLEIN: Thank you, Your Honor.

12:45:13 19 MR. ELIKAN: Thank you, Your Honor.

12:45:13 20 (The noon recess was taken.)

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12:45:15 1 RENO, NEVADA, TUESDAY, JANUARY 28, 2020, 1:27 P.M.

12:45:15 2 ---oo---

12:45:15 3

01:27:39 4 THE COURT: Please be seated.

01:27:40 5 All right. When we recessed, I asked counsel to

01:27:44 6 confer on the disputed exhibits.

01:27:47 7 Do you have a resolution?

01:27:50 8 MR. SIPES: Your Honor, I'm not sure. This is

01:27:52 9 Christopher Sipes on behalf Amarin.

01:27:54 10 We had proposed -- this all arose this Saturday

01:27:57 11 night when we received this exhibit. We're not in a position

01:28:00 12 to commit what we could collect. Apparently, a lot of it is,

01:28:04 13 we think, may be third-party vendors, so we can't quite get

01:28:07 14 it.

01:28:07 15 What we would propose is to allow the admission

01:28:10 16 of the information relating to Dr. Toth and Dr. Budoff, but we

01:28:15 17 would then have the opportunity tomorrow, since we haven't had

01:28:18 18 an opportunity, to put things in through an actual

01:28:21 19 knowledgeable custodian, just submit as part of the record a

01:28:24 20 couple of articles that would explain the accuracy of the CMS

01:28:29 21 website and what the problems are.

01:28:30 22 But, Mr. Klein has indicated they do not want to

01:28:34 23 agree to that.

01:28:34 24 MR. KLEIN: Your Honor, our position -- we'll

01:28:37 25 defer to the Court, but our position is that either Amarin

01:28:40 1 should come up with what the numbers are, it's in Amarin's
01:28:43 2 possession, and then we'll work with them and submit something
01:28:46 3 to let you know what the numbers are, or, you should just go
01:28:50 4 ahead and rule.

01:28:51 5 THE COURT: Well, I'm going to rule. I'm going
01:28:53 6 to give Amarin, though, the opportunity to present evidence
01:28:55 7 that Mr. Sipes just indicated.

01:28:58 8 So, I'm going to -- I've already admitted
01:29:04 9 DX 3017 and 3018. I will admit 3000 to 3005, but with all the
01:29:13 10 information redacted other than Dr. Toth and Dr. Budoff.

01:29:18 11 Now, the reason I'm allowing Dr. Budoff is
01:29:21 12 because I'm going to give Amarin the opportunity to present
01:29:23 13 the information that Mr. Sipes indicated. Otherwise, I would
01:29:26 14 exclude that portion as well, and, I will admit the summary
01:29:32 15 exhibit which is 3006.

01:29:32 16 (Defendants' Exhibits 3000 through 3006
01:29:35 17 received in evidence.)

01:29:35 17 MR. SIPES: Thank you.

01:29:36 18 MR. KLEIN: Thank you, Your Honor.

01:29:38 19 THE COURT: Are you ready for redirect?

01:29:40 20 MR. ELIKAN: Sure.

01:29:41 21 THE COURT: All right.

01:29:41 22 REDIRECT EXAMINATION

01:29:41 23 BY MR. ELIKAN:

01:29:42 24 Q Dr. Toth, do you recall you were questioned about von
01:29:46 25 Schacky on cross-examination?

01:29:47 1 A Yes, counsel.

01:29:48 2 Q And you were asked about Table 1?

01:29:51 3 A Yes.

01:29:52 4 MR. ELIKAN: I want to ask you about some other
01:29:53 5 portions of the article. Can we have DX 1605 at page 2. I
01:30:02 6 want to pull up the title "Method" and the paragraph below.

01:30:02 7 BY MR. ELIKAN:

01:30:07 8 Q What does von Schacky indicate here about how he found
01:30:10 9 the articles to include in his review?

01:30:12 10 A He performed a Medline search, and he also used
01:30:18 11 publications from a Cochrane review, and, also used articles
01:30:24 12 from his personal library.

01:30:26 13 Q Does it appear to you to be a reasonably thorough review
01:30:30 14 of the literature?

01:30:32 15 A Well, when you refer to Medline and Cochrane review, I
01:30:36 16 would say yes.

01:30:40 17 MR. ELIKAN: Can we have the von Schacky paper,
01:30:42 18 PX 905 and -- oh, you already have it on the screen.

01:30:42 19 BY MR. ELIKAN:

01:30:47 20 Q Let me ask you, you were asked about other passages in
01:30:52 21 von Schacky as well. I want to talk about a passage on
01:30:57 22 page 5.

01:30:57 23 MR. ELIKAN: Can we have page 5, Mr. Brooks?

01:30:57 24 BY MR. ELIKAN:

01:31:01 25 Q Is that the passage you were asked about? And it appears

01:31:04 1 in the left-hand column.

01:31:06 2 A EPA and versus DHA, yes.

01:31:11 3 Q And I want to look little above that, the bottom of
01:31:17 4 page 4, to the lower right-hand corner. Do you see the
01:31:20 5 heading "Effects on Other Lipids"?

01:31:22 6 A Yes.

01:31:22 7 Q And under this heading it discusses the effects of fish
01:31:26 8 oil on serum lipids. That's in the line right below the
01:31:30 9 title, right?

01:31:31 10 A Yes, counsel.

01:31:32 11 Q And I want to look below that to the heading, "DHA-EPA"
01:31:40 12 in the right-hand column with page 4. EPA-DHA.

01:31:46 13 A I see it.

01:31:47 14 Q Okay. And that column then -- that section continues on
01:31:51 15 to the next page, right?

01:31:52 16 A Yes.

01:31:52 17 Q And that is immediately above the passage that you were
01:31:58 18 asked about.

01:31:58 19 A Yes.

01:31:59 20 Q Okay. I want to look at the first full sentence that
01:32:02 21 starts, "Rather consistently..."

01:32:06 22 A "LDL has" --

01:32:07 23 MR. ELIKAN: Can we highlight that, Mr. Brooks.

01:32:07 24 BY MR. ELIKAN:

01:32:14 25 Q And what does von Schacky here say?

01:32:18 1 A "Rather consistently, LDL has been seen to be
01:32:21 2 increased with a few exceptions. This may be due to
01:32:25 3 the fact that the more buoyant" --
01:32:26 4 Q Hold on. I'm just asking about that sentence. It seems
01:32:30 5 like it's going on to other issues here.
01:32:31 6 What does this sentence state, if anything, about
01:32:35 7 the absolute effect of both EPA and DHA on LDL?
01:32:39 8 A That the tendency is for it to -- that the tendency for
01:32:44 9 LDL is to increase in response to exposure to both omega-3s.
01:32:49 10 Q Does that support the table, Table 1 -- which I would
01:32:53 11 like to return to now, it's at page 9.
01:32:56 12 A It does support the table.
01:32:57 13 Q And how so?
01:32:59 14 A Because in the table, both EPA and DHA are associated
01:33:03 15 with a single upgoing arrow.
01:33:07 16 Q And I believe you testified on direct as well about the
01:33:12 17 von Schacky reference in Table 1?
01:33:15 18 A Yes.
01:33:15 19 Q And is it the case that of the different parameters, to
01:33:21 20 the extent they vary, they favor DHA?
01:33:25 21 A Yes.
01:33:25 22 Q Let me ask you a question you haven't been asked and --
01:33:32 23 A There's a question I haven't been asked yet?
01:33:35 24 Q Would any person of ordinary skill in the art want to
01:33:39 25 make Lovaza worse?

01:33:42 1 A Of course not.

01:33:49 2 MR. ELIKAN: I want to talk to you, now, about
01:33:51 3 the Saito article. Can we have DX1547, and I want to turn to
01:33:59 4 page 5, and can we pull up on the screen the second paragraph
01:34:03 5 in the right-hand column.

01:34:03 6 BY MR. ELIKAN:

01:34:09 7 Q Do you see in the first sentence Saito reports, risk
01:34:12 8 reduction by 53 percent was achieved in JELIS in what he calls
01:34:19 9 the high TG, low HDL-C group?

01:34:22 10 A Yes, counsel.

01:34:23 11 MR. ELIKAN: Okay. I want to look at how high
01:34:27 12 TG and low HDL-C was defined.

01:34:30 13 Can we go to the bottom of page 2, and I want to
01:34:34 14 grab the last paragraph, and then the five categories on the
01:34:39 15 next page. So, the "furthermore."

01:34:39 16 BY MR. ELIKAN:

01:34:52 17 Q And which of these is the high TG, low HDL-C group.

01:34:56 18 A Number 4.

01:34:58 19 Q And is that a group that is severely
01:35:02 20 hypertriglyceridemic?

01:35:03 21 A No, counsel.

01:35:04 22 Q Explain.

01:35:07 23 A Well, the triglyceride of greater than or equal to 150,
01:35:14 24 that is the cut point for defining hypertriglyceridemia.

01:35:24 25 And these authors do provide a mean and a standard

01:35:28 1 deviation for this group on triglycerides. But, of course,
01:35:32 2 very high triglycerides would be above 500.

01:35:34 3 Q Is this group even close to a patient population with
01:35:38 4 very high triglycerides?

01:35:39 5 A No, sir.

01:35:41 6 MR. ELIKAN: Now, I want to turn to Table 1 on
01:35:44 7 page 4. And can we highlight the title of the table.

01:35:44 8 BY MR. ELIKAN:

01:35:50 9 Q What does the title indicate is in this table?

01:35:52 10 A "Patient Background Factors At Time of Registration, and
01:35:56 11 Triglyceride and HDL Cholesterol Levels."

01:35:59 12 Q Now, I want to look at the bottom of the table under
01:36:02 13 lipid profile. Does this table provide the mean triglyceride
01:36:06 14 and LDL-C levels for those Saito designates as the high
01:36:11 15 triglyceride, low HDL-C patients?

01:36:15 16 A Yes.

01:36:15 17 Q And what's the mean for LDL-C?

01:36:18 18 A It's 200 -- the mean for LDL-C?

01:36:22 19 Q Correct.

01:36:22 20 A Is 186.

01:36:24 21 Q And the mean for triglyceride?

01:36:25 22 A 272.

01:36:28 23 Q Does it also provide a range of triglyceride levels for
01:36:32 24 patients in that group?

01:36:33 25 A Yes, 207 to 399.

01:36:36 1 Q Again, this isn't a patient population of very high
01:36:41 2 triglycerides, right?

01:36:42 3 A No, counsel.

01:36:45 4 MR. ELIKAN: Can we have PDX 6-7, please.

01:36:45 5 BY MR. ELIKAN:

01:36:54 6 Q Based on their LDL-C and triglyceride levels, which group
01:36:58 7 on PDX 6-7 is the high TG, low LDL-C group in Saito most like?

01:37:05 8 A The mixed dyslipidemia with a mean of approximately 232,
01:37:13 9 the farthest one to the left.

01:37:16 10 Q You testified earlier that the prior art showed that in a
01:37:19 11 population with very high triglycerides, the approved
01:37:24 12 triglyceride-lowering agents raised LDL-C while lowering
01:37:28 13 triglycerides, right?

01:37:29 14 A Yes.

01:37:29 15 Q Based on review of Saito 2008, would the person of
01:37:33 16 ordinary skill have had any reason to believe that patients
01:37:36 17 with very high triglycerides would avoid an increase in LDL-C
01:37:41 18 after administration of EpaDEL?

01:37:43 19 A No.

01:37:49 20 MR. ELIKAN: Let's turn to Yokoyama, DX 1553,
01:37:53 21 and I want to go to page 8, and I want to highlight the last
01:37:58 22 sentence in the last paragraph.

01:37:58 23 BY MR. ELIKAN:

01:38:04 24 Q What does Yokoyama have to state here about whether the
01:38:07 25 results observed in JELIS can be expected in other countries?

01:38:11 1 A Well, they note that,

01:38:13 2 "Because their population was exclusively

01:38:15 3 Japanese, we cannot generalize our results to other

01:38:18 4 populations. We need to investigate whether EPA is

01:38:21 5 effective for prevention of major coronary events in

01:38:25 6 hypercholesterolemic patients without or with

01:38:28 7 coronary artery disease in other countries."

01:38:32 8 MR. ELIKAN: Let's go back to Saito, DX 1547.

01:38:37 9 And I want to go to page 2 in the left-hand column.

01:38:37 10 BY MR. ELIKAN:

01:38:41 11 Q In the second paragraph under "Introduction," six lines

01:38:45 12 down in the middle paragraph, what does this state -- if we

01:38:49 13 can highlight "from and EPA suppressed CAD" until the end of

01:38:54 14 that sentence. What does this state about the eating habits

01:38:58 15 of the patients who were studied?

01:39:00 16 A "EPA suppressed coronary artery disease even

01:39:06 17 in Japanese hypercholesterolemic patients who

01:39:15 18 routinely consume a large amount of EPA and DHA from

01:39:19 19 fish."

01:39:22 20 Q And what, if anything, does this indicate about whether

01:39:25 21 Saito -- I'm sorry.

01:39:28 22 What, if anything, does this indicate about whether

01:39:31 23 JELIS, as seen by Dr. Saito, was actually measuring the

01:39:38 24 effects of pure EPA in a population?

01:39:41 25 A Well, he appears to be thinking that supplemental EPA on

01:39:47 1 top of dietary EPA and DHA appears to suppress CAD.

01:39:52 2 Q Is there any indication in Saito that the same results

01:39:57 3 could be obtained -- would be obtained by administering pure

01:40:01 4 EPA to a population that was not already taking in large

01:40:05 5 amounts of DHA as part of their fish diet?

01:40:08 6 A No.

01:40:09 7 Q During your direct examination, we looked at a Cochrane

01:40:15 8 collaboration, PX 953. I want to take a look at that now.

01:40:22 9 And I believe this is the reference that you

01:40:25 10 testified concluded in 2018 that Omega-3 fatty acids are

01:40:31 11 probably not useful for preventing or treating cardiovascular

01:40:37 12 disease. Do I have that right?

01:40:39 13 A Yes.

01:40:40 14 Q Let's go to page 74.

01:40:43 15 And do you see that the right-hand column lists

01:40:47 16 materials considered relating to JELIS?

01:40:49 17 A Yes.

01:40:50 18 Q And if we look at the bottom, under JELIS 2007, what do

01:40:59 19 we see there?

01:41:00 20 A It's the Saito reference that we have been discussing

01:41:05 21 from Atherosclerosis in 2008.

01:41:08 22 Q DX 1547?

01:41:09 23 A Yes.

01:41:10 24 Q Does this indicate that the Saito article was considered

01:41:14 25 by the authors before reaching their conclusion that Omega-3

01:41:19 1 fatty acids are probably not useful for preventing or treating
01:41:28 2 cardiovascular disease?

01:41:29 3 A Yes.

01:41:30 4 Q On cross-examination, you were also asked questions about
01:41:39 5 Dr. Bays' article about the Marine trial?

01:41:43 6 A Yes.

01:41:43 7 Q DX 1741. So, I want to look a little bit closer at the
01:41:50 8 passage you were shown on cross.

01:41:52 9 MR. ELIKAN: Can we have page 7, right column,
01:41:57 10 the first full paragraph, beginning with "in several small
01:42:01 11 studies..."

01:42:01 12 BY MR. ELIKAN:

01:42:03 13 Q First, do you see that the first sentence provides a
01:42:06 14 citation to five different studies, concluding that both EPA
01:42:12 15 and DHA lowered triglyceride levels?

01:42:15 16 A Yes.

01:42:15 17 Q And those are references 4, 5, and 14 through 16?

01:42:19 18 A Yes.

01:42:20 19 MR. ELIKAN: Okay. Let's go to page 9, and can
01:42:25 20 we blow-up reference 14.

01:42:25 21 BY MR. ELIKAN:

01:42:31 22 Q What's the date of publication of reference 14?

01:42:34 23 A 2009.

01:42:37 24 Q Does citation to this reference indicate that the
01:42:40 25 statement made by Dr. Bays was informed by later publications

01:42:45 1 predating March 2008; or, instead, informed as well by later
01:42:51 2 events and publications?

01:42:53 3 A By later events and publications.

01:42:55 4 Q Let's go back to the same paragraph we were looking at on
01:42:59 5 page 7.

01:43:01 6 Do you see a citation after the next sentence,

01:43:07 7 "However, although DHA treatment generally
01:43:10 8 increased LDL cholesterol levels, EPA therapy did
01:43:15 9 not"?

01:43:15 10 A I see it.

01:43:16 11 Q Is there a citation after that sentence?

01:43:19 12 A No, counsel.

01:43:20 13 Q In reading this section of the paragraph as a whole,
01:43:25 14 before the discussion in the Marine trial, which follows
01:43:28 15 below, is there a primary citation that Dr. Bays uses to
01:43:32 16 support his understanding of prior experience with EPA and
01:43:35 17 DHA?

01:43:36 18 A No.

01:43:38 19 Q Which article is cited to most often in that paragraph?

01:43:52 20 A Uh --

01:43:53 21 Q I just want the reference number. Do you see a reference
01:43:56 22 to --

01:43:56 23 A Yes, there is -- 17 appears twice.

01:43:59 24 Q So do you understand that to be the primary citation he
01:44:02 25 uses to support his understanding of prior experience with EPA

01:44:08 1 and DHA in this paragraph?

01:44:10 2 A Yes, sir.

01:44:11 3 Q And let's turn to page 9, the left column. And let's
01:44:14 4 look at reference 17.

01:44:18 5 When was it published?

01:44:19 6 A That's a paper by Ernie Schaefer, in Circulation in 2010.

01:44:24 7 Q Not available in 2008?

01:44:26 8 A No, I don't believe it would be, no.

01:44:30 9 Q Does reliance on that reference indicate that the
01:44:34 10 statements made by Dr. Bays were informed by events and
01:44:38 11 publications post-dating March 2008?

01:44:41 12 A Post-dating 2008.

01:44:43 13 Q Let's go back to page 7, and I want to look at the
01:44:50 14 paragraph we were looking at before.

01:44:54 15 All right. The sentence, "in several small previous
01:44:57 16 studies..."

01:45:07 17 And if we look down a little bit further, do you see
01:45:11 18 that that links up to another sentence beginning, "These
01:45:15 19 previous studies..."

01:45:17 20 A Yes.

01:45:19 21 Q And looking further down in that sentence, "These
01:45:24 22 previous studies," what does Dr. Bays say about the population
01:45:30 23 studied in these previous studies?

01:45:32 24 A He notes,

01:45:33 25 "These previous studies were generally in

01:45:35 1 patients with normal to borderline high triglyceride
01:45:39 2 levels, and none included patients with very high
01:45:42 3 triglyceride levels, namely, greater than
01:45:46 4 500 milligrams per deciliter."

01:45:48 5 Q Let's look at the last sentence. Does Dr. Bays say that
01:45:54 6 the results achieved were confirmatory or something else?

01:46:00 7 A They were not confirmatory. It was an unexpected finding
01:46:05 8 that Vascepa or AMR101 produced no significant increase in the
01:46:11 9 LDL cholesterol levels.

01:46:16 10 MR. ELIKAN: Can we have DX 1578 at page 1. Can
01:46:33 11 we blow-up Table 1.

01:46:33 12 BY MR. ELIKAN:

01:46:40 13 Q Looking at the title, do you recall being shown this on
01:46:43 14 cross-examination?

01:46:44 15 A I do, counsel.

01:46:46 16 Q And what was the -- can you describe the patient
01:46:50 17 population in Table 1. Was it -- specifically, was it one
01:46:55 18 with very high triglycerides or not?

01:46:57 19 A It was not.

01:46:59 20 Q How does Table 1 describe the patient population?

01:47:04 21 A The baseline triglycerides for the Lovaza and simvastatin
01:47:08 22 group had a baseline 268, and the placebo and simvastatin
01:47:14 23 group had a baseline triglyceride of 271.

01:47:20 24 MR. ELIKAN: Can we go DX 1553 at page 3.

01:47:25 25 So, this is the Yokoyama study that you were

01:47:28 1 asked about.

01:47:31 2 Can we blow-up the serum lipid levels in the
01:47:37 3 left-hand side.

01:47:37 4 BY MR. ELIKAN:

01:47:57 5 Q Doctor, looking at these units of measurements -- they're
01:48:02 6 in millimoles per liter -- but can you tell whether these --
01:48:05 7 can you tell approximately what the milligrams per deciliter
01:48:10 8 equivalents are?

01:48:12 9 A Yes. For the LDL it would have been approximately 184;
01:48:17 10 for triglycerides it was, in the EPA group, 153; and in the
01:48:23 11 placebo group, 154.

01:48:31 12 Q What types -- what type of patients, then, does the JELIS
01:48:35 13 study concern?

01:48:36 14 A Well, they were specifically labeled as
01:48:39 15 hypercholesterolemic patients, and with LDLs -- Japanese
01:48:45 16 patients especially, with LDLs of 183, that's a remarkably
01:48:49 17 high mean, mean baseline LDL for a Japanese population, and
01:48:56 18 their triglycerides were, essentially, the mean was near
01:48:59 19 normal.

01:49:02 20 Q So, again, not a patient population with very high
01:49:06 21 triglycerides?

01:49:07 22 A No. There weren't any patients with very high
01:49:11 23 triglycerides as the Saito article showed us where the maximal
01:49:15 24 triglyceride was actually 399.

01:49:17 25 Q And I'm not sure I followed your answer fully a couple of

01:49:29 1 answers ago. Is this a patient population that you would
01:49:34 2 describe as hypercholesterolemic or something else?

01:49:40 3 A Yes, hypercholesterolemic.

01:49:44 4 MR. ELIKAN: Can we have D -- can I ask you to
01:49:47 5 put up DDX 10.90. Is that okay? Thank you very much?

01:49:57 6 THE CLERK: Are you asking for defense
01:49:58 7 litigation tech to do that?

01:50:01 8 MR. ELIKAN: Yes, because we don't have their
01:50:03 9 slides.

01:50:03 10 THE CLERK: Okay. Let me transfer it over.

01:50:06 11 MR. ELIKAN: Oh. Thank you very much.

01:50:08 12 And thank you.

01:50:08 13 BY MR. ELIKAN:

01:50:10 14 Q Do you recall being shown this slide before?

01:50:14 15 A No.

01:50:18 16 Q Well, I assure you were shown it on cross-examination --

01:50:22 17 A Okay. I do now.

01:50:23 18 Q Now you do.

01:50:24 19 And you were referred to the highlighted matter. I
01:50:28 20 want to ask you about the last sentence in the 2017 Vascepa
01:50:34 21 Operating Plan, specifically -- I shouldn't say the last
01:50:38 22 sentence, the last sentence that's called out in this cutout.

01:50:43 23 What does is say there?

01:50:45 24 A That Vascepa being LDL neutral and other efficacy
01:50:50 25 messages are also very relevant.

01:51:02 1 MR. ELIKAN: Let's go to DX 1524, WO '118, and I
01:51:10 2 want to go to -- oh, I'm sorry. We have to switch over.
01:51:14 3 And thank you once again.
01:51:17 4 Can we go to page 4, the middle of the page.
01:51:17 5 BY MR. ELIKAN:
01:51:38 6 Q Do you see in the middle of the page a description of --
01:51:43 7 if we can scroll down a little bit -- I'm sorry. I'm on the
01:51:53 8 wrong page. It's page 7 of the exhibit.
01:52:05 9 Do you see a statement,
01:52:09 10 "There has been reported in the -- there has
01:52:13 11 also been reported in the Heart Failure Society of
01:52:16 12 America 2005 Annual Meeting that based on such
01:52:21 13 action, such high purity EPA-E was expected to have
01:52:25 14 the effects of improving cardiovascular events in
01:52:30 15 Hyperlipidemia patients.,
01:52:33 16 And combined use with HMG-CoA RI was
01:52:38 17 effective in inhibiting cardiac events in a large
01:52:42 18 scale clinical trial".
01:52:43 19 A Yes.
01:52:44 20 Q And then immediately below an identification of that
01:52:47 21 trial as the JELIS trial.
01:52:58 22 Do you see that, it says, "In this large clinical
01:53:01 23 trial of JELIS"?
01:53:01 24 A I do, counsel.
01:53:03 25 Q And remind me, in the context of W -- this is WO '118,

01:53:09 1 **but what were the baseline triglycerides in the JELIS study?**

01:53:13 2 A **The baseline triglyceride value in the EPA group was**

01:53:18 3 **153 milligrams per deciliter, and in the placebo arm,**

01:53:22 4 **154 milligrams per deciliter.**

01:53:24 5 Q **And the baseline LDL-C?**

01:53:27 6 A **Approximately 183.**

01:53:28 7 Q **Are those patients with very high triglycerides?**

01:53:31 8 A **No.**

01:53:32 9 Q **Anywhere close?**

01:53:35 10 A **Not even close. And Saito did mention that the highest**

01:53:43 11 **triglyceride value observed in JELIS was 399.**

01:53:54 12 MR. ELIKAN: **Can we go to page 12 now, and the**

01:53:59 13 **paragraph under "Merits of the Invention."**

01:53:59 14 BY MR. ELIKAN:

01:54:04 15 Q **Do you see that it says, "The invention contains at least**

01:54:08 16 **EPA"?**

01:54:09 17 A **Yes.**

01:54:09 18 Q **And what does that mean?**

01:54:11 19 A **Well, that would suggest that there are other components**

01:54:14 20 **in the capsule.**

01:54:18 21 Q **And it says it's effective --**

01:54:21 22 A **Yes, as --**

01:54:22 23 Q **-- in preventing occurrence of cardiovascular events in**

01:54:25 24 **hypercholesterolemia patients.**

01:54:29 25 A **Yes.**

01:54:29 1 Q What exactly are those?

01:54:34 2 A And are we still talking about JELIS here?

01:54:38 3 Q Well, you can give me a general definition, and then we

01:54:41 4 can -- I can ask you about JELIS as well.

01:54:44 5 A Sure.

01:54:44 6 Q But what hypercholesterolemia patients?

01:54:48 7 A Well, they would be patients who have LDL levels higher

01:54:52 8 than what their risk stratum would -- that they would be

01:54:57 9 higher than where you would want them to be based on their

01:55:04 10 risk strata.

01:55:06 11 Q Are they different or the same as a very high

01:55:09 12 triglyceride patient population?

01:55:09 13 A Oh, they're different.

01:55:11 14 MR. ELIKAN: Let's go to page 25, and I want to

01:55:17 15 highlight the sentence at the bottom of the page beginning

01:55:20 16 with, "another preferable fatty acid."

01:55:20 17 BY MR. ELIKAN:

01:55:25 18 Q What is that other preferable fatty acid in WO '118?

01:55:30 19 A It's DHA.

01:55:32 20 Q And what does the passage go on to say about ratio?

01:55:36 21 A It says,

01:55:37 22 "While the compositional ratio of EPA over

01:55:43 23 DHA, content of EPA and DHA, in the total fatty acid

01:56:00 24 and dosage of EPA plus DHA, are not particularly

01:56:03 25 limited. As long as intended effects of the present

01:56:07 1 invention are attained, the composition is preferably
01:56:12 2 the one having a purity of EPA and DHA, for example,
01:56:16 3 the one having --"

01:56:17 4 Q Doctor, I think you missed a word. It says "high
01:56:20 5 purity," is that right?

01:56:23 6 A "The composition is preferably the one having
01:56:27 7 a high purity of EPA and DHA, for example, the one
01:56:31 8 having a proportion of the EPA plus DHA in the total
01:56:36 9 fatty acid and derivatives thereof, of preferably
01:56:42 10 40 percent by weight or higher."

01:56:45 11 Q Would you like me to keep reading?

01:56:47 12 A Nope. That's good.

01:56:59 13 MR. ELIKAN: I'd like to go to page 35 now, and
01:57:28 14 can you highlight, please, the sentence beginning with "the
01:57:33 15 soft capsule product," and you can continue all the way down
01:57:44 16 through the paragraph.

01:57:44 17 BY MR. ELIKAN:

01:57:48 18 Q What does this have to say here about whether you can use
01:57:50 19 Omacor or Lovaza with this invention?

01:57:53 20 A It says,

01:57:54 21 "The soft capsule, Omacor, containing about
01:57:59 22 46 percent by weight of EPA, and about 38 percent by
01:58:03 23 weight of DHA, is commercially available in the U.S.,
01:58:07 24 Europe, and other countries, as a drug applied for
01:58:11 25 hypertriglyceridemia."

01:58:13 1 Q Does that mean can you use Omacor with this invention?

01:58:17 2 A Yes.

01:58:17 3 Q Do you recall being asked about Hayashi, as well, on
01:58:34 4 cross-examination?

01:58:35 5 A Yes, counsel.

01:58:35 6 Q I want to take a look at your definition of the
01:58:40 7 credentials of the person of ordinary skill in the art and
01:58:44 8 compare them to Dr. Heinecke's.

01:58:46 9 MR. ELIKAN: Can we have your PDX 6-13? Can we
01:58:52 10 put it next, Mr. Brooks, to DDX 6.10.

01:58:52 11 BY MR. ELIKAN:

01:59:00 12 Q And these are the two sets of credentials that you and
01:59:03 13 Dr. Heinecke testified about, correct?

01:59:05 14 A Yes.

01:59:06 15 Q Looking at these definitions, do either you or
01:59:12 16 Dr. Heinecke understand the person of ordinary skill in the
01:59:16 17 art to be a statistician?

01:59:18 18 A No.

01:59:18 19 Q Or as having advanced training in statistics?

01:59:23 20 A No.

01:59:24 21 Q So would the person of ordinary skill in the art,
01:59:28 22 irrespective of which set of credentials is accepted by the
01:59:34 23 Court, be essentially viewing Hayashi from the perspective of
01:59:38 24 a clinician?

01:59:40 25 A Yes.

01:59:40 1 Q Not a statistician.

01:59:41 2 A No.

01:59:42 3 Q Now, you were shown a snippet of deposition testimony

01:59:46 4 relating to Dr. Lavin's declaration.

01:59:50 5 A Yes.

01:59:50 6 Q The deposition was of Dr. Lavin, do you recall that?

01:59:54 7 A I do.

01:59:56 8 Q And you saw that he testified he could have written

01:59:59 9 his -- he would have written his declaration differently if he

02:00:03 10 could; is that right?

02:00:06 11 A Yes.

02:00:06 12 Q And in the course of forming your opinions in this case,

02:00:08 13 did you read the entirety of that deposition at one time?

02:00:14 14 A At one time.

02:00:15 15 Q Did he later provide additional testimony about whether

02:00:19 16 he would have written his declaration differently?

02:00:22 17 A He did.

02:00:23 18 MR. ELIKAN: Can we have on the screen pages

02:00:29 19 110, 11 -- line 11, through page 111, line 12.

02:00:35 20 And these, Your Honor, have been admitted as

02:00:37 21 part of the deposition designations in this case.

02:00:37 22 BY MR. ELIKAN:

02:00:44 23 Q And can you read this, please, to yourself, Doctor, and

02:00:48 24 then I'm going ask a question.

02:00:50 25 A From where to where? The whole thing here?

02:00:53 1 Q Yes.

02:00:55 2 A (Witness complies.)

02:01:20 3 Okay, counsel.

02:01:22 4 Q Do you see he says -- and this is later in the

02:01:25 5 deposition, I'll represent to you, that his calculations

02:01:27 6 represent his best estimate?

02:01:29 7 A Yes.

02:01:29 8 Q Considering both this passage, and the one you looked at

02:01:32 9 earlier on cross-examination, do you understand Dr. Lavin to

02:01:37 10 have clearly admitted that he erred in his statistical

02:01:43 11 calculations?

02:01:44 12 A That he clearly erred?

02:01:50 13 He notes here it was the best estimate that he could

02:01:52 14 come up with given that he only had data parameters, the mean

02:01:56 15 and the standard deviation. I think what he's alluding to

02:02:00 16 there is he would have needed the raw data to perform a better

02:02:05 17 analysis.

02:02:05 18 Q Setting aside the issues surrounding Dr. Lavin's

02:02:09 19 declaration, to your knowledge, was any statistical analysis

02:02:13 20 of Hayashi publically available as of March 2008?

02:02:18 21 A No.

02:02:19 22 Q And whether or not there were a few patients with higher

02:02:24 23 triglycerides than recorded in -- I think it was Figure 2, is

02:02:29 24 that right?

02:02:29 25 A Yes. Figure 2.

02:02:32 1 Q -- that we talked about on direct examination, is there
02:02:34 2 anything in Hayashi that provides posttreatment LDL-C levels
02:02:41 3 for any individuals over 500?

02:02:44 4 A No.

02:02:44 5 Q You were shown a slide with some articles in which Amarin
02:03:03 6 provided some assistance in writing -- in your articles. Can
02:03:07 7 you describe what Amarin's role was.

02:03:11 8 A So the papers that Mr. Klein showed all addressed
02:03:20 9 research in the Optum database, which is a national healthcare
02:03:27 10 database, and we published a series of papers looking at the
02:03:33 11 impact of hypertriglyceridemia on risks from a broad spectrum
02:03:40 12 of cardiovascular events.

02:03:42 13 And Amarin provided the statistical support with a
02:03:47 14 statistician at Optum. They also paid for the folks at Optum
02:03:55 15 to run the numbers. They paid for publication charges, and
02:04:02 16 then we did have editorial assistance.

02:04:05 17 Q Were they in charge of the final content of the article,
02:04:10 18 so that we look at those and don't see that they're your
02:04:15 19 opinions but, instead, those of Amarin's?

02:04:17 20 A No. My colleagues and I had complete academic freedom.
02:04:24 21 We were not steered in one direction or another. The data
02:04:29 22 were the data.

02:04:37 23 MR. ELIKAN: Is it possible to switch over to
02:04:41 24 your box there? And if I could ask, once again, for your
02:04:43 25 assistance.

02:04:45 1 Could we have DDX 10.92?

02:04:45 2 BY MR. ELIKAN:

02:04:49 3 Q Do you recall being asked about DX 3009 and this passage

02:04:54 4 from the article that you wrote?

02:04:57 5 A I didn't write this. This was --

02:05:00 6 Q I'm sorry. You're absolutely --

02:05:01 7 A This was an interview.

02:05:03 8 Q This is the interview. Okay.

02:05:05 9 A Apparently, this was an interview at the American

02:05:07 10 Diabetes Scientific Sessions in 2018.

02:05:11 11 Q And what there are you saying about the JELIS trial and

02:05:15 12 the level of triglycerides of those patients?

02:05:20 13 A "If the patient's primary residual issue is

02:05:24 14 elevated triglyceride, there is support from the

02:05:26 15 JELIS trial which demonstrated that the addition of

02:05:30 16 EPA to ongoing statin therapy, particularly in

02:05:33 17 patients with triglycerides over 150, incurred

02:05:35 18 benefit."

02:05:36 19 There, I was referring to the Saito paper.

02:05:38 20 Q And, again, what -- is that patient population one that

02:05:42 21 has -- that has very high triglycerides?

02:05:45 22 A No. The highest triglyceride value was 399 in that

02:05:50 23 subgroup analysis.

02:05:58 24 Q And was there something comparable to the MARINE study

02:06:04 25 studying Epaedel and showing, demonstrating that in very high

02:06:08 1 triglyceride patients, there's no rise in LDL-C?

02:06:12 2 A No.

02:06:19 3 Q And if you wanted to replicate these results in JELIS or
02:06:24 4 Saito, in a lower triglyceride population, but in a country
02:06:33 5 that doesn't eat quite as much fish, would you want to add
02:06:38 6 DHA, or just use pure EPA?

02:06:41 7 A You would want to add DHA because the DHA in the Japanese
02:06:47 8 diet was already so high, and fish contains a lot of DHA.

02:06:52 9 Q During cross-examination, you were asked numerous times
02:07:06 10 about LDL-C, and it was described in the questioning as a side
02:07:11 11 effect.

02:07:13 12 Before MARINE, did a person of ordinary skill in the
02:07:17 13 art see the rise in LDL-C in -- while reducing triglycerides
02:07:22 14 in a very high triglyceride patient population as a general
02:07:28 15 phenomenon or as a side effect?

02:07:31 16 A It was a general phenomenon.

02:07:47 17 MR. ELIKAN: Let's turn to LIPITOR and the
02:07:51 18 statins. Can we go to PX 989.

02:08:05 19 Oh, I'm sorry. I forgot to ask you to switch it
02:08:09 20 over. I apologize. Thanks once again.

02:08:29 21 I want to see what ATP III has to say about
02:08:32 22 statins and their ability to lower LDL-C.

02:08:36 23 Can we go to page 108, and I want to bring up
02:08:40 24 the very high triglyceride section in the bottom of Table
02:08:46 25 7.2-4.

02:08:56 1 MR. SIPES: What page?

02:09:04 2 MR. ELIKAN: Sorry. Your Honor, I've got the

02:09:06 3 wrong page. I'll get the right one momentarily.

02:09:12 4 Thank you, Mr. Brooks.

02:09:14 5 So we're on page 190. And can we look, again,

02:09:17 6 at Table 7.2-1, and the entry for very high triglycerides at

02:09:23 7 the bottom. Page 194.

02:09:23 8 BY MR. ELIKAN:

02:10:24 9 Q And do you see the heading Treatment Considerations For

02:10:28 10 Elevated Serum Triglycerides?

02:10:31 11 A I do.

02:10:32 12 Q And we've looked at this table before, right?

02:10:36 13 A Yes.

02:10:36 14 Q And we discussed goals of therapy?

02:10:38 15 A Yes.

02:10:38 16 Q I would like to look at what the ATP III had to say about

02:10:42 17 statins. Is there a line for statins here?

02:10:45 18 A Yes, there is.

02:10:47 19 MR. ELIKAN: Can we highlight that, Mr. Brooks.

02:10:51 20 Sorry. Lower on down, under "very high triglycerides."

02:10:51 21 BY MR. ELIKAN:

02:10:59 22 Q And for very high triglycerides, what does the ATP III

02:11:03 23 have to say about statins?

02:11:06 24 A "Not first line agent for very high

02:11:08 25 triglycerides, statins not powerful triglyceride

02:11:12 1 **lowering drugs."**

02:11:13 2 **Q Is that consistent with your own clinical experience?**

02:11:16 3 **A Yes, it is.**

02:11:17 4 **Q And is that why, in some of the papers that**

02:11:36 5 **we've seen, statins are given along with a true**

02:11:40 6 **triglyceride-lowering agent?**

02:11:41 7 **A Yes.**

02:11:42 8 **Q And are statins approved to treat very high**

02:11:56 9 **triglycerides?**

02:11:57 10 **A No.**

02:11:59 11 **MR. ELIKAN: Can we have PX 486, the Bays 2008**

02:12:06 12 **paper.**

02:12:15 13 **One moment, Your Honor.**

02:12:15 14 **BY MR. ELIKAN:**

02:12:28 15 **Q In looking at page 2, the bottom left, do you see a**

02:12:34 16 **sentence starting, "Statins and ezetimibe..."**

02:12:40 17 **A Yes.**

02:12:41 18 **Q And what does Dr. Bays have here to say about statins?**

02:12:48 19 **A "Statins and ezetimibe are approved lipid**

02:12:51 20 **altering drugs that may modestly reduce triglyceride**

02:12:55 21 **levels."**

02:12:56 22 **Q And what do you understand from the word "modestly"?**

02:12:58 23 **A Well, it would be suboptimal or it's not a very**

02:13:02 24 **significant effect.**

02:13:03 25 **Q And do you see after that it says, Dr. Bays says, "They**

02:13:10 1 are mainly used to lower LDL cholesterol, LDL-C levels?"

02:13:15 2 A Yes.

02:13:18 3 Q Is that consistent with your clinical experience?

02:13:18 4 A Yes.

02:13:18 5 Q Does Dr. Bays go on to report what agents are useful to

02:13:24 6 reduce triglyceride levels?

02:13:27 7 A Yes.

02:13:28 8 Q Which ones? What does he have to say?

02:13:31 9 A He notes that other lipid altering agents that are used

02:13:37 10 more specifically to reduce triglyceride levels include

02:13:41 11 niacin, fibrates, and omega-3 fatty acids.

02:13:45 12 Q And are those the agents that were available in 2008

02:13:50 13 specifically to reduce triglycerides in a very high

02:13:55 14 triglyceride population?

02:13:56 15 A Yes.

02:14:05 16 MR. ELIKAN: Is it possible to do that switch

02:14:07 17 thing again?

02:14:08 18 THE CLERK: Absolutely.

02:14:09 19 MR. ELIKAN: Thank you very much.

02:14:11 20 Could we have DDX 8.8.

02:14:11 21 BY MR. ELIKAN:

02:14:32 22 Q I'll represent to you that this was defendants'

02:14:35 23 demonstrative that they used while examining Mr. Hofmann, an

02:14:41 24 economist, a few days ago.

02:14:46 25 Based on what we've been discussing, do you have an

02:14:49 1 understanding as to why there is no LIPITOR or other statin in
02:14:55 2 this market share analysis of triglyceride reducing drugs?

02:15:00 3 MR. KLEIN: Objection, Your Honor. This is
02:15:01 4 beyond the scope of my cross.

02:15:05 5 MR. ELIKAN: It's squarely within the scope of
02:15:07 6 the cross. The cross was trying to establish that LIPITOR and
02:15:11 7 other statins were a triglyceride-lowering agent. It's
02:15:14 8 inconsistent with the position taken by Mr. Hofmann. It's
02:15:18 9 spot-on the cross.

02:15:22 10 MR. KLEIN: Your Honor, I went through the
02:15:23 11 LIPITOR label, and it says what it is, and it is approved for
02:15:27 12 patients above 500. I don't know what that has to do with
02:15:30 13 this prescription share analysis which I never used.

02:15:33 14 THE COURT: I agree, Mr. Klein, you didn't use
02:15:36 15 this DDX 8.8, but I assume the point that's made here is
02:15:41 16 consistent with this line of redirect, and, that is, that
02:15:44 17 statin is not used to reduce TG levels.

02:15:49 18 Is that right? I mean, that's what you're
02:15:51 19 trying to ask the witness.

02:15:52 20 MR. ELIKAN: That's right. It's really not even
02:15:55 21 considered a triglyceride reducing agent, other than with the
02:15:58 22 limited utility that was pointed to in ATP III and in
02:16:03 23 Dr. Bays' article.

02:16:05 24 THE COURT: But what you're using this
02:16:06 25 demonstrative for is to ask Dr. Toth if he knows why this

02:16:11 1 chart doesn't include statins. Is that asking him to
02:16:17 2 speculate why somebody prepared a chart?

02:16:21 3 MR. ELIKAN: No. I'm asking him whether has he
02:16:22 4 an understanding as to whether a statin is part of the
02:16:26 5 triglyceride-lowering or reducing drug market, and that, as a
02:16:31 6 physician who has ready access to different
02:16:34 7 triglyceride-reducing drugs will know full-well what the
02:16:37 8 options are.

02:16:38 9 THE COURT: All right. I'm sustaining the
02:16:40 10 objection. I'm not going to allow the doctor to testify as to
02:16:43 11 this demonstrative.

02:16:44 12 He certainly can testify as to what his
02:16:46 13 understanding is as a treating physician and what's available
02:16:50 14 in the market, which I think he's testified to repeatedly.

02:17:03 15 So if you want to ask him the question without
02:17:06 16 the chart, you may do so.

02:17:08 17 MR. ELIKAN: I'm going to move on, Your Honor.

02:17:08 18 BY MR. ELIKAN:

02:17:11 19 Q Let's go back to the Bays' article, PX 486, and I want to
02:17:19 20 look at page 9 under the heading, "Statins and P-OM3"
02:17:27 21 prescription omega-3 fatty acids, "Reduce Triglyceride Levels
02:17:31 22 By Different Mechanisms."

02:17:32 23 Do you see that heading?

02:17:34 24 A Yes.

02:17:35 25 Q And is it correct that statins and omega-3 fatty acids

02:17:41 1 **reduce triglycerides by different mechanisms?**

02:17:44 2 A **Yes.**

02:17:49 3 Q **Are statins HMG-CoA inhibitors?**

02:17:56 4 A **Yes.**

02:17:58 5 Q **And do they inhibit cholesterol biosynthesis?**

02:18:03 6 A **They sure do.**

02:18:04 7 Q **Does that lead to increased clearance of LDL from the**

02:18:08 8 **blood?**

02:18:09 9 A **It does.**

02:18:09 10 Q **And do you see that Dr. Bays says,**

02:18:16 11 "Up-regulated LDL receptors may also increase

02:18:20 12 clearance of other TG-containing lipoproteins at

02:18:24 13 least partially accounting for the modest TG lowering

02:18:28 14 effects of statins"?

02:18:30 15 A **I do see that.**

02:18:31 16 Q **Is there any evidence that either EPA or DHA inhibits**

02:18:41 17 **HMG-CoA?**

02:18:43 18 A **No, there's no evidence for that.**

02:18:44 19 Q **And whatever EPA and DHA do, is it fair to say they don't**

02:18:49 20 **act like statins?**

02:18:50 21 A **Yes.**

02:19:05 22 MR. ELIKAN: **I would like to go DX 3007.**

02:19:14 23 **Can we go to page 15.**

02:19:18 24 THE COURT: **Are you looking at -- are you asking**

02:19:20 25 **to switch the monitor?**

02:19:22 1 MR. ELIKAN: Oh, I'm so sorry.

02:19:25 2 THE COURT: That's okay.

02:19:26 3 MR. ELIKAN: Yes. Sorry.

02:19:29 4 And can we have the paragraph two up from the

02:19:33 5 **Table, Mr. Brooks.** "LIPITOR has not been studied..."

02:19:45 6 What does the LIPITOR label here report?

02:19:49 7 A "LIPITOR has not been studied in conditions

02:19:51 8 where the major lipoprotein abnormality is elevation

02:19:56 9 of chylomicrons, Fredrickson Types I and V."

02:20:07 10 Q I believe you've testified about this already, but we

02:20:13 11 call this HLP V; is that right?

02:20:16 12 A Yes. That -- yes, it would be HLP V.

02:20:20 13 Q And is that the same as very high triglycerides?

02:20:23 14 A Yes.

02:20:27 15 Q I want to look at the table you were shown. That's on

02:20:33 16 page 12, Table 9 -- I'm sorry, I'm on page 21. I know it's

02:21:02 17 **Table 9.**

02:21:17 18 Let's go to pages 11 and 12, then, that's where

02:21:25 19 **Table 4** is?

02:21:33 20 Do you see for Atorvastatin, 10 milligrams, N equals

02:21:33 21 37?

02:21:50 22 A Yes.

02:21:51 23 Q What are the numbers right below that? The minus 41, and

02:21:51 24 then it has something in parentheses.

02:21:57 25 A Minus 76.2 and 49.4.

02:22:04 1 Q Is that the range of response?

02:22:09 2 A Yes.

02:22:09 3 Q That mid max percent change from baseline?

02:22:12 4 A Yes.

02:22:12 5 Q And if we look at the 80-milligram, what is that range of

02:22:15 6 response?

02:22:15 7 A For 80 milligrams, it was minus 60 to minus

02:22:26 8 13.8 percent -- I'm sorry, minus 82 and up to 41.3.

02:22:32 9 Q And there was N equals 14?

02:22:34 10 A Yes.

02:22:34 11 Q Does this indicate that Atorvastatin is well controlling

02:22:39 12 the triglycerides, or not?

02:22:44 13 A No. It's pretty bizarre that you would see a 40 and

02:22:50 14 50 percent elevation, at least in one patient, in the

02:22:54 15 triglyceride. It's not an effect you would want to see.

02:23:11 16 MR. ELIKAN: One moment, Your Honor.

02:23:15 17 At this time, no more questions, Your Honor.

02:23:22 18 MR. KLEIN: Your Honor, may I have a brief

02:23:24 19 recross?

02:23:25 20 THE COURT: Yes.

02:23:27 21 RECROSS-EXAMINATION

02:23:27 22 BY MR. KLEIN:

02:23:38 23 Q Dr. Toth, do you remember on redirect counsel asked you

02:23:42 24 about Dr. Bays' 2011 article on MARINE?

02:23:46 25 A Yes.

02:23:47 1 Q And, in particular, he pointed you to the sentence in the
02:23:51 2 article that said that the LDL neutral effects seen were an
02:23:56 3 unexpected finding?

02:23:58 4 A Yes, counsel.

02:23:58 5 Q Okay. And for the record, I'm referring to DX 1741.

02:24:03 6 Are you aware that Dr. Bays was rather ambivalent
02:24:08 7 about that particular language?

02:24:10 8 A I'm not aware that he was ambivalent about it.

02:24:14 9 MR. KLEIN: Okay. Let's go to DX 1740. And
02:24:20 10 let's -- first, let's start in the bottom e-mail.

02:24:20 11 BY MR. KLEIN:

02:24:27 12 Q Okay. And you see this is an e-mail to -- Dr. Bays'
02:24:33 13 first name is Harold, right?

02:24:34 14 A Yes, it is.

02:24:35 15 Q And you can see this is an e-mail from someone at Amarin
02:24:39 16 to Dr. Bays?

02:24:40 17 A Yes.

02:24:40 18 Q Okay. And they are sending Dr. Bays the manuscript for
02:24:46 19 what became the 2011 article, and they said,

02:24:49 20 "Please see the latest version attached. We
02:24:52 21 have made a minor tweak at the top of page 15. This
02:24:56 22 is very important for Amarin. We can give you a call
02:24:59 23 if you wish to explain it. Otherwise, if this change
02:25:04 24 is acceptable to you, please let us know. The paper
02:25:08 25 is being cleaned up more, and full references added

02:25:11 1 after which it will be distributed to the other
02:25:14 2 co-authors by tonight as we discussed."

02:25:17 3 Do you see that?

02:25:18 4 A I do.

02:25:19 5 MR. KLEIN: Okay. Let's go to the top and
02:25:21 6 blow-up doctor -- the -- yeah, that's fine.

02:25:21 7 BY MR. KLEIN:

02:25:27 8 Q Okay. You see Dr. Bays is responding here?

02:25:30 9 A I do.

02:25:31 10 Q And he says, "Rene, I am rather ambivalent regarding the
02:25:35 11 below."

02:25:36 12 Do you see that?

02:25:37 13 A Yes.

02:25:37 14 Q And the below is quoted from the manuscript.

02:25:40 15 And you can see, if you look at the last sentence,
02:25:43 16 it says,

02:25:44 17 "The unexpected finding in the current trial
02:25:47 18 was that AMR 101 did not increase LDL levels, no
02:25:53 19 statistically significant change."

02:25:54 20 Do you see that?

02:25:55 21 A I do.

02:25:56 22 MR. KLEIN: And if you take off that last
02:25:58 23 highlighting, Mr. Gross.

02:25:58 24 BY MR. KLEIN:

02:26:01 25 Q I don't know if you can see it, but it looks like

02:26:03 1 "unexpected" was highlighted in the original. Do you see it's
02:26:08 2 a little -- there's, like, a dark box around "unexpected"?

02:26:11 3 A Yes.

02:26:12 4 Q Okay. And so Dr. Bays goes on to say,
02:26:14 5 "However, please be aware that the statement
02:26:17 6 below, 'that this finding was unexpected,' in quotes,
02:26:21 7 "is in contradiction to the rest of the manuscript.
02:26:25 8 My initial sense is that it largely guts the current
02:26:28 9 storyline of the paper, and the reality of this drug
02:26:31 10 development program."

02:26:33 11 Is this an e-mail that Amarin had shown you in
02:26:36 12 connection with this case?

02:26:38 13 A A long time ago. I recall it now.

02:26:42 14 MR. KLEIN: Okay. No further questions, Your
02:26:42 15 Honor.

02:26:44 16 THE COURT: Is that e-mail admitted yet, 1740?

02:26:47 17 MR. KLEIN: Yes, it came in with designations.

02:26:51 18 THE COURT: All right. Thank you.

02:26:52 19 MR. ELIKAN: Your Honor, I have a few brief
02:26:55 20 questions.

02:26:57 21 THE COURT: You want to do a re-redirect based
02:26:59 22 on the recross?

02:27:02 23 MR. ELIKAN: That was my intention.

02:27:04 24 THE COURT: I'm going to permit brief
02:27:06 25 re-redirect and re-recross if needed.

1 REDIRECT EXAMINATION

2 **BY MR. ELIKAN:**

3 Q You were just shown an e-mail, and my question to you is
4 whether you know whether there were any further exchanges
5 between Dr. Bays and Amarin about this sentence, whether by
6 e-mail or telephone.

7 A I do not.

8 Q Are you in a position to put yourself in his head and
9 determine what he meant by the statements he made in his
10 e-mail?

11 A Of course I'm not.

12 Q Did Dr. Bays, and the other authors, ultimately decide to
13 include the sentence about an unexpected finding in the final
14 manuscript?

15 A It is in the paper.

16 MR. ELIKAN: I want to look at the article
17 itself. Can we have DX 1741. Can we look at the bottom and
18 see when it was published. The bottom of the
19 abstract actually -- or that will work, too.

20 THE WITNESS: In 2011.

21 MR. ELIKAN: And can we scroll up to the end of
22 the abstract?

23 **BY MR. ELIKAN:**

24 Q What journal was this published in?

25 A The American Journal of Cardiology.

02:28:21 1 Q Have you served as a peer reviewer for that journal?

02:28:24 2 A Yes.

02:28:25 3 Q In your experience, does it maintain a rigorous peer

02:28:27 4 review process?

02:28:28 5 A It does.

02:28:29 6 Q Based on the final manuscript, does it appear that the

02:28:34 7 peer reviewers insisted on the removal of the sentence?

02:28:38 8 A No.

02:28:38 9 Q We discussed during your direct examination an Editor's

02:28:53 10 Roundtable, PX 833.

02:28:53 11 A Yes.

02:28:55 12 Q In which doctor --

02:28:55 13 THE COURT: Does this now exceed the scope of

02:28:59 14 the re-recross?

02:29:01 15 MR. ELIKAN: This goes exactly into Dr. Bays'

02:29:04 16 mindset, so I think it's squarely --

02:29:05 17 THE COURT: This witness already testified he

02:29:08 18 can't go into Dr. Bays' mindset.

02:29:11 19 MR. ELIKAN: Well, Dr. Bays is very clear about

02:29:13 20 his mindset in the Editor's Roundtable.

02:29:14 21 THE COURT: Then the document will speak for

02:29:16 22 itself.

02:29:20 23 MR. ELIKAN: I guess, then, there are no further

02:29:23 24 questions.

02:29:23 25 THE COURT: Thank you.

02:29:23 1 Mr. Klein, do you have any?

02:29:25 2 MR. KLEIN: I do not, Your Honor.

02:29:26 3 THE COURT: All right. Thank you.

02:29:27 4 Dr. Toth, that means you may be excused.

02:29:30 5 THE WITNESS: Thank you so much, Your Honor.

02:29:48 6 (The witness was excused.)

02:29:48 7 MR. SIPES: Your Honor, we have no further live

02:29:51 8 witnesses. We just have some deposition excerpts to move in.

02:29:56 9 My colleague, Alaina Whitt, will do that.

02:29:59 10 MS. WHITT: As Mr. Sipes mentioned, we have some

02:30:04 11 final deposition designations to submit from Peter Mathers and

02:30:09 12 Howard Weintraub, and with those designations we have a few

02:30:13 13 exhibits to also move into evidence, if I may read those off.

02:30:18 14 There's just about ten.

02:30:19 15 THE COURT: Yes, Ms. Whitt.

02:30:21 16 MS. WHITT: Okay. So we're starting with PX

02:30:23 17 289, which is the same as DX 1701. So we'll move both of

02:30:27 18 those in together;

02:30:28 19 Same goes for PX 572 and DX 1678;

02:30:34 20 PX 573 and DX 1681;

02:30:40 21 PX 776 and DX 1682.

02:30:47 22 And those are all for the deposition of Peter

02:30:50 23 Mathers.

02:30:51 24 And then we have two exhibits for the deposition

02:30:54 25 of Howard Weintraub, and those are DX 1897 and DX 1906.

02:31:02 1 And I would also note --

02:31:04 2 THE COURT: So just those two exhibits for --

02:31:08 3 MS. WHITT: For Dr. Weintraub's designations,

02:31:11 4 yes. So those are the exhibits that we would move in.

02:31:15 5 THE COURT: And then you started to say more,

02:31:17 6 and I interrupted you.

02:31:19 7 MS. WHITT: I can wait until those are moved

02:31:21 8 into evidence.

02:31:21 9 THE COURT: Are you moving those into evidence?

02:31:24 10 MS. WHITT: Yes, please.

02:31:25 11 THE COURT: Is there any objection?

02:31:27 12 MR. KLEIN: No objection.

02:31:28 13 THE COURT: All right. The motion is granted.

02:31:28 14 (Plaintiffs' Exhibits 289, 572 and 573
02:31:28 received in evidence.)

02:31:28 15 (Defendants' Exhibits 1701, 1678, 1682,
02:31:32 16 1897 and 1906 received in evidence.)

02:31:32 16 MS. WHITT: And then just one final note that

02:31:34 17 we'll be submitting the final transcripts for all of the

02:31:37 18 designations that have been submitted in court -- or during

02:31:40 19 trial, and those will have links to the exhibits that have

02:31:43 20 also been admitted, and we'll be submitting those tomorrow.

02:31:48 21 THE COURT: All right. Thank you.

02:31:50 22 MS. SUN: Your Honor, this is Caroline Sun for

02:31:56 23 defendants. At this time, defendants would like to offer the

02:31:59 24 designated deposition testimony of Aaron Berg into the record.

02:32:04 25 There are no exhibits to move in.

02:32:07 1 And it is my understanding that our paralegal
02:32:10 2 will drop off a flash drive before the close of business
02:32:14 3 today.

02:32:15 4 THE COURT: Thank you.

02:32:15 5 Any objection?

02:32:17 6 MR. SIPES: No objections, Your Honor.

02:32:19 7 THE COURT: All right. The motion is granted.

02:32:20 8 All right. Does the plaintiff rest then?

02:32:28 9 MR. SIPES: Yes, Your Honor. We close our
02:32:30 10 rebuttal case.

02:32:31 11 THE COURT: Okay. Thank you.

02:32:33 12 Do defendants have rebuttal witnesses to offer?

02:32:35 13 MR. KLEIN: No, Your Honor.

02:32:36 14 THE COURT: Ms. Huttner, is that correct?

02:32:38 15 MS. HUTTNER: Yes, Your Honor, it is.

02:32:39 16 THE COURT: All right. Then the evidence is in.

02:32:45 17 I have some housekeeping matters, and then I
02:32:48 18 want to ask counsel about what I had promised to do in terms
02:32:52 19 of issuing the bench order.

02:32:54 20 Mr. Sipes, you had indicated that Amarin would
02:32:57 21 like to offer some articles or some additional information to
02:33:01 22 give context to the exhibits that I admitted, the 3000 to 3005
02:33:10 23 series of exhibits.

02:33:11 24 MR. SIPES: That's correct.

02:33:11 25 THE COURT: What do you plan to offer?

02:33:13 1 MR. SIPES: We plan to offer a couple of
02:33:15 2 articles that discuss what is included in the CMS open
02:33:18 3 payments report and the reliability of that report, and we
02:33:21 4 will get them to you by tomorrow.

02:33:23 5 THE COURT: I'm anticipating that if there's an
02:33:26 6 objection -- or if Mr. Klein and his colleague want to address
02:33:32 7 any issue raised by these additional exhibits, how I would
02:33:35 8 resolve them. So do you have an idea of what you would be
02:33:38 9 offering?

02:33:39 10 MR. SIPES: My colleague, Mr. Kennedy, is more
02:33:42 11 familiar what we will be offering, and Mr. Elikan. But, I
02:33:46 12 believe it's a number of published articles on the CMS open
02:33:50 13 payments.

02:33:55 14 We can send it to defendants in advance of
02:33:58 15 submitting it to the Court, Your Honor.

02:33:59 16 THE COURT: Yes. Thank you.

02:34:00 17 And I'll permit Mr. Klein and his colleague to
02:34:03 18 offer any response, and I'll consider -- give the information
02:34:07 19 whatever weight it deserves in the bench order.

02:34:09 20 MR. SIPES: Thank you, Your Honor.

02:34:11 21 THE COURT: So the deadline for you to submit
02:34:13 22 the articles will be tomorrow, and then I will give Mr. Klein
02:34:16 23 and Ms. Huttner -- what's tomorrow, Wednesday?

02:34:20 24 THE CLERK: Yes.

02:34:21 25 THE COURT: -- until Monday to respond.

02:34:34 1 Next, I know that I need to resolve -- do I need
02:34:38 2 to resolve the issue of sealing any exhibits? I know I kept
02:34:43 3 deferring that until the end of the trial.

02:34:45 4 MR. SIPES: Yes, Your Honor. We would like the
02:34:47 5 opportunity to redact some of the exhibits before they're put
02:34:50 6 in a public exhibit room.

02:34:53 7 We would -- and I think we haven't done that,
02:34:56 8 Your Honor, but we can also, tomorrow, submit a list of the
02:35:00 9 exhibits we would like the opportunity to redact.

02:35:02 10 THE COURT: I would like for the process to be
02:35:04 11 clearer because we're talking about extensive exhibits, and I
02:35:07 12 did not keep track to look at the bottom which has been
02:35:10 13 designated as confidential.

02:35:12 14 I assumed -- so this is the process. Unless I
02:35:15 15 see a designation to seal, I assume everything else is
02:35:19 16 unsealed.

02:35:20 17 For the designation to seal, I want a list that
02:35:25 18 includes the exhibit number, the relevant page, a sentence
02:35:33 19 stating why it should be -- compelling reason exists to seal,
02:35:40 20 and if there's a dispute by the other side that it shouldn't
02:35:45 21 be seal, then a sentence responding why it shouldn't be
02:35:48 22 sealed.

02:35:49 23 I don't think -- because of the number of
02:35:51 24 exhibits, I'm trying to make this less burdensome. My concern
02:35:55 25 is if you actually submit the redacted version, it's going to

02:35:58 1 be pretty onerous.

02:36:00 2 So let's try that process first. Just the list
02:36:03 3 and I can look through -- if it becomes too difficult for me,
02:36:08 4 I'll let you know.

02:36:09 5 MR. SIPES: All right. Thank you.

02:36:10 6 THE COURT: And the same for -- I don't know if
02:36:12 7 the defendants have any exhibits that you've designated that
02:36:14 8 you think should be sealed.

02:36:15 9 MS. HUTTNER: I don't believe so, Your Honor.

02:36:17 10 THE COURT: All right. So it will just be on
02:36:19 11 Amarin's part to submit their information, and I would like
02:36:21 12 the information -- well, I'll give you more time since -- how
02:36:27 13 much time do you need?

02:36:30 14 MR. SIPES: Can we -- next week, Your Honor?

02:36:33 15 Could we do it sometime towards the end of next week.

02:36:36 16 THE COURT: Next Friday.

02:36:37 17 MR. SIPES: That sounds great.

02:36:40 18 THE COURT: Well, you need to give the list to
02:36:43 19 defense counsel to review first. So, you have until next
02:36:47 20 Friday to give the other side the list.

02:36:48 21 And then -- so next Friday will be February 7th,
02:36:57 22 and I would like to know -- so do the -- Amarin will provide
02:37:05 23 defense counsel the list of exhibits and what will be proposed
02:37:10 24 to be redacted and the reason, by February 7th.

02:37:17 25 And I will give defense counsel until

02:37:19 1 **February 14th -- well, you have until February 12th to**
02:37:24 2 **respond. If there's still any disagreement that still needs**
02:37:27 3 **to be resolved, then both sides will submit the information to**
02:37:32 4 **the Court by February 14th.**

02:37:34 5 So, what I'd like to know is I want to get the
02:37:36 6 **information by February 14th so I have a deadline.**

02:37:47 7 As I said, I want to avoid as much redaction as
02:37:50 8 **necessary. I don't want the bench order to be sealed. So,**
02:37:53 9 **that's my goal. If I refer to exhibits that are redacted, I**
02:37:57 10 **probably wouldn't seal the order anyway.**

02:38:00 11 MR. SIPES: And, Your Honor, I'm pretty
02:38:02 12 **confident that what we will be redacting will not be portions**
02:38:05 13 **of documents that were discussed in open court.**

02:38:07 14 THE COURT: Thank you.

02:38:08 15 That leads me to when the bench order needs to
02:38:13 16 **be issued. I realize -- I think -- I'm trying to think back**
02:38:16 17 **to what I agreed to do. I thought I remembered a March -- the**
02:38:20 18 **end of March date.**

02:38:21 19 Is that when I should have the bench order
02:38:23 20 **issued, by the end of March, or is it earlier?**

02:38:26 21 MR. SIPES: I recall March 31st, Your Honor.

02:38:28 22 MS. HUTTNER: Yeah.

02:38:29 23 MR. SIPES: But, I won't speak for the
02:38:30 24 **defendants.**

02:38:30 25 MS. HUTTNER: I think Your Honor had mentioned

02:38:30 1 that you had some issue with the court administration or the
02:38:35 2 age of the case in selecting that. But that's my
02:38:38 3 recollection.

02:38:38 4 THE COURT: I don't remember. I just remember
02:38:40 5 March 31st as the date.

02:38:41 6 MS. HUTTNER: That's what I heard as well.

02:38:43 7 THE COURT: I don't recall counsel proposed --
02:38:46 8 requesting post-trial briefs.

02:38:48 9 MR. SIPES: I think we would like some form of
02:38:50 10 post-trial brief or post-trial findings of fact and
02:38:53 11 conclusions of law.

02:38:54 12 THE COURT: Did you submit any proposed
02:38:57 13 deadline?

02:38:58 14 I'm getting trials mixed up. I have another
02:39:01 15 trial coming up in two weeks where there are actually
02:39:02 16 deadlines proposed from the date of the transcript becomes
02:39:02 17 available. So I'm trying to -- I don't want to get the two
02:39:06 18 cases mixed up.

02:39:08 19 So, here's what I would like to do. I think it
02:39:10 20 would be -- I know you may like to have a post-trial brief.
02:39:14 21 What would be very helpful for me is -- as I said, the
02:39:16 22 pretrial brief I found to be very helpful to give me the
02:39:19 23 framework and the issues that I was supposed to be thinking
02:39:22 24 about in listening to evidence at trial, so thank you for
02:39:25 25 doing that.

02:39:25 1 But proposed findings are also helpful, and I'm
02:39:29 2 going to ask you to do one more thing with respect to the
02:39:31 3 proposed findings, which will save me a lot of time, and that
02:39:34 4 is that you cite to the record that's now available because I
02:39:38 5 always endeavor to cite to the record to support my proposed
02:39:42 6 finding.

02:39:43 7 So the order is going to consist, in the
02:39:46 8 proposed findings of fact section, facts that I may take from
02:39:50 9 one party or the other, depending on who I agree with -- for
02:39:54 10 the most part, you agree on a lot of things -- and then I want
02:39:57 11 to offer a citation to the trial to support that finding.

02:40:01 12 So if you want to revise your proposed findings
02:40:04 13 and cite to the record, that would be much appreciated.

02:40:09 14 And if you think it's necessary to have a
02:40:12 15 closing -- a closing brief to present the arguments that you
02:40:19 16 want to present, I will permit that as well. But, I don't
02:40:22 17 want to delay that for too long because I don't want to forget
02:40:25 18 what I've heard so far in the last few weeks.

02:40:28 19 So I would set that deadline from the date the
02:40:31 20 official transcript becomes available, but I don't know when
02:40:34 21 we would have a time for that.

02:40:38 22 What do you think? What's your timeframe?

02:40:41 23 MR. SIPES: That sounds good to us. I'm not
02:40:44 24 sure when the final transcript will be due. But, we were
02:40:47 25 thinking something along the lines of the -- each party submit

02:40:51 1 its post-trial findings of fact, conclusions of law on, say,
02:40:55 2 the 14th -- if I have the Friday right. So, that would leave
02:40:58 3 Valentine's Day evening free.

02:41:02 4 And then a post-trial brief that would then be
02:41:05 5 submitted a week later, so that would give us a chance, as
02:41:08 6 well, to comment on each side's proposed findings of fact,
02:41:12 7 conclusions of law, which if I'm doing the math right, would
02:41:14 8 be the 21st.

02:41:15 9 THE COURT: If I give you the 13th to submit
02:41:18 10 post-trial proposed findings, would that give you enough time?

02:41:22 11 MR. SIPES: I think so, Your Honor.

02:41:23 12 THE COURT: I don't know when -- do you have --
02:41:25 13 I know you have the rough transcript. I don't know if you
02:41:28 14 have the official transcript though.

02:41:29 15 MR. SIPES: We have two. The first two days are
02:41:31 16 in final, I believe, and we will probably be conferring if
02:41:35 17 there are any errata. But we have the first two days.

02:41:38 18 But I think the 13th for the post-trial proposed
02:41:41 19 findings of fact and conclusions of law would be fine. That
02:41:46 20 should make Valentine's Day a little better.

02:41:46 21 MS. HUTTNER: My only concern is when the final
02:41:48 22 transcript will be available.

02:41:49 23 MR. SIPES: But I think we can probably start
02:41:52 24 working from the redacted so long as we think we might get the
02:41:55 25 final in a week?

02:41:56 1 THE COURT: I don't know. Let's ask.

02:41:56 2 (Conversation with the court reporter and the

02:43:07 3 Court held off the record.)

02:43:07 4 MR. SIPES: Your Honor, if it would help, we

02:43:09 5 have a proposal, if it works for the Court, which would be to

02:43:11 6 submit our post-trial findings of fact and conclusions of law

02:43:14 7 two weeks after we get the final, and then the brief one week

02:43:18 8 thereafter, and that way, we'll just work from whenever the

02:43:25 9 final becomes available.

02:43:30 10 THE COURT: If we follow that schedule -- so two

02:43:36 11 weeks after the final, let's assume that you have the final by

02:43:39 12 February 7th, two weeks would be the 21st, and then you would

02:43:43 13 propose the closing -- well, why would you need to delay the

02:43:49 14 closing briefs?

02:43:50 15 MR. SIPES: To have the opportunity to review

02:43:51 16 the other side's proposed findings of fact and conclusions of

02:43:56 17 law, and comment on that as well.

02:43:57 18 THE COURT: So that everything would be

02:43:59 19 submitted by the end of February? That would give me then the

02:44:01 20 month of March.

02:44:13 21 All right. I'll approve that schedule.

02:44:15 22 But even though I'm going to set the deadline

02:44:18 23 for filing the proposed findings two weeks from when the

02:44:22 24 official transcripts are filed, essentially, I'm not going to

02:44:28 25 extend that deadline.

02:44:29 1 So I'm hoping the court reporter would have the
02:44:32 2 transcript ready for you. You may get less than two weeks.
02:44:34 3 I'm going to change the proposal. Proposed
02:44:36 4 findings with citations would be submitted on February 14th --
02:44:40 5 sorry, Mr. Sipes. Hopefully, they'll be done before then,
02:44:44 6 before the 14th, Valentine's Day, and the closing briefs are
02:44:49 7 due on the 28th. And I will make sure that I follow-up to see
02:44:55 8 that you get the transcripts within that time.

02:44:59 9 MR. SIPES: So it will be the 14th and the 28th,
02:45:01 10 Your Honor?

02:45:02 11 THE COURT: Yes.

02:45:03 12 MR. SIPES: Perfect.

02:45:07 13 MR. KLEIN: Your Honor, may I ask a point of
02:45:08 14 clarification?

02:45:09 15 THE COURT: Yes.

02:45:09 16 MR. KLEIN: So for the proposed findings, I take
02:45:13 17 it you're asking more than we just add cites to what we had
02:45:18 18 said before. If there are additional findings based on what
02:45:21 19 happened at trial, would you like us to revise what we already
02:45:26 20 submitted?

02:45:27 21 THE COURT: I think that's fair.

02:45:29 22 MR. KLEIN: Okay.

02:45:30 23 MR. SIPES: That's fine.

02:45:30 24 THE COURT: And, of course, if there are
02:45:32 25 findings you don't think are necessary, you could remove them,

02:45:35 1 too.

MR. KLEIN: That's true, too.

02:45:37 3 THE COURT: All right. Is there anything else,
02:45:38 4 then, that I need to address before I recess today?

MS. HUTTNER: Nothing from DRL, Your Honor.

MR. KLEIN: Nothing from Hikma. Thank you.

MR. SIPES: Nothing from Amarin.

02:45:53 8 THE COURT: For the proposed findings of fact
02:45:55 9 with citations, in addition to filing them, would you also
02:45:59 10 submit a Word version to Miss Clerk. It will make it easier
02:46:03 11 on me.

02:46:04 12 MR. SIPES: I guess, Your Honor, there is one
02:46:06 13 question I have, which is whether you have a page limit in
02:46:09 14 mind for the post-trial brief.

02:46:10 15 THE COURT: Yes. There's always a page limit.

MR. SIPES: That's why I thought I'd ask.

02:46:15 17 THE COURT: I think it was 30 pages for the
02:46:17 18 opening brief. I hope you don't exceed the 30 pages, but I'll
02:46:23 19 give you 30 pages.

02:46:24 20 MR. SIPES: Thank you, Your Honor.

02:46:26 21 THE COURT: There's no limit on the proposed
02:46:28 22 findings of fact.

02:46:32 23 Actually, why don't you, in addition to
02:46:43 24 submitting the Word version of the proposed findings, go ahead
02:46:47 25 and submit the Word version of your post-trial briefs.

02:46:49 1 Because if you agree on the standard, I'll probably just take
02:46:52 2 your legal standard and so on, so it will make it easy as
02:46:56 3 well.

02:46:56 4 MR. SIPES: Fine.

02:46:57 5 THE COURT: Which, actually, I think we started
02:46:59 6 to do anyway with the opening pref.

02:47:00 7 All right. Is there anything else I need to
02:47:02 8 address?

02:47:03 9 MR. SIPES: No, Your Honor.

02:47:03 10 THE COURT: Thank you, counsel. I want to thank
02:47:05 11 everyone for making this trial, with voluminous documents, so
02:47:08 12 seamless.

02:47:09 13 And I want to thank you for being so patient
02:47:11 14 with my schedule and the fact you didn't get consecutive days.
02:47:14 15 But you've all been exemplary and professional, and for that,
02:47:19 16 I thank you.

02:47:19 17 MR. SIPES: Thank you, Your Honor.

02:47:19 18 MS. HUTTNER: Thank you, Your Honor.

02:47:22 19 MR. KLEIN: Thank you, Your Honor.

02:47:22 20 (Court adjourned.)

21 -00-

22 I certify that the foregoing is a correct
23 transcript from the record of proceedings
in the above-entitled matter.

24 /s/Kathryn M. French 2/4/2020
25 Kathryn M. French, CCR #392, RPR
Official Reporter

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9	Redirect Examination by Mr. Elikan	1981

9 PLAINTIFF'S EXHIBITS:

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11	572 and 573	1984
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13 PLAINTIFFS' DEMONSTRATIVE EXHIBITS:

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15 DEFENDANTS' EXHIBITS:

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